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THE BIOLOGICAL EFFECTS OF SHORT RADIATIONS

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I

FOR a generation, X-rays and radium radiations have been used in medicine and in biology for the purpose of injuring certain cells or tissues without permanently harming other parts of the organism. With their aid the radiotherapist may temporarily or even permanently check the unruly growth of neoplasms; the biologist may produce abnormal conditions in an organ or cell for the purpose of studying its normal functions. In both cases the end result rather than the process by which the result is obtained, has been the important matter under consideration. For this reason very little attention has been paid to the events which take place in cells from the moment that irradiation begins until the more obvious microscopic changes appear. But without doubt, information on this point is of highest importance; indeed, the little that we now know has thrown much light on many important radiological problems.

To find out what occurs in cells during and after irradiation it is first necessary to study the morphological changes. Much of this work has already been done; the histological effects are fairly well known, and while there may be some disagreement in respect to details, the broad outlines of the degenerative processes are well recognized. This work is purely descriptive, in itself it gives little insight into the real nature of the changes or their cause. But a more careful examination of the finer details reveals reactions which have previously been overlooked. These are concerned with the changes in the chemical constituents of protoplasm. And at this point the biologist must rely on the chemist for a correct interpretation of the phenomena. To be sure, analysis has thus far proved so difficult that little is known about the various transformations which occur in the proteins, fats, and carbohydrates as a result of irradiation, but undoubtedly the much needed facts will gradually be obtained. Finally, the changes which can be observed, whose chemical nature is beginning to be known, are produced by the transformation of radiant energy in the cell. In order to picture the mechanism by which these changes are brought about we must rely on physical facts and assumptions. Indeed, a successful biological experiment with these radiations must be made with the help of a physicist who can arrange prop-

erly the conditions of exposure and make the essential measurements. These three sciences, then, must contribute to the solution of the problem of what takes place in a cell as the result of irradiation.

X-rays and radium radiations are especially valuable in biological research because of their ability to penetrate deeply into cells in which they may affect some particular region without causing irreparable damage to the rest. This differential action is not due to any selective power of the rays; they do not give up their energy and thus produce an effect in the sensitive regions only, while passing through the resistant portions without stopping. All parts of the cell and all kinds of cells have about the same power of absorption; whether they are injured or not depends on their physiological condition at the time of exposure and afterward. But the factors which are responsible for this condition are thus far practically unknown.

Sensitivity to radiations is sometimes spoken of as though it were a peculiar phenomenon, different from general sensitivity. This is quite incorrect; cells that are susceptible to X-rays and to radium are also susceptible to other stimuli. During mitosis they are more easily injured by agents of very different kinds than they are at any other moment. But these radiations differ from heat, cold, and chemical action in that they can bring to light small differences in susceptibility not readily shown by other means. And they do this with the expenditure of an exceedingly small amount of energy which is absorbed by only an infinitestimal proportion of the atoms in the irradiated material. But the effect of such absorption is great. As much energy as will warm a cup of cold water would, if absorbed in the form of penetrating radiations, kill a man. In this respect their action is analogous to that of an active poison, such as ricin, which even in very minute quantities is fatal.

Nor have the radiations any power to produce effects of a novel kind; the degenerative changes which follow an exposure to X-rays or to radium are not new to pathologists. Heat, cold, the electric current, and many chemicals bring about the same type of injuries. This does not mean that the mode of action on protoplasm is the same; in all probability it differs greatly, but the end result is alike in all cases.

The lively interest in the effects which these short radiations produce on living cells and organisms may be realized from the fact that an abstract journal which reviews only investigations on these topics, together with those on ultraviolet and visible light, cites upwards of 5000 titles each year. Of these more than half deal directly with medical problems of diagnosis and treatment, but a large proportion of the remainder has to do with the morphological, physiological, and chemical changes produced in protoplasm by penetrating radiations.

In this review I shall discuss some of the topics which are engaging the attention of radiologists at the present time, omitting all reference to the very extensive literature on the action of ultraviolet rays, the visible spectrum, and of mitogenic rays. And I shall emphasize the results which throw light on the reaction of the cell rather than those which are concerned with the entire organism. For the behavior of the organism after irradiation is a result of the direct action of the rays plus many secondary responses which greatly complicate the total effect. It is obviously impossible to treat the subject in detail, or to cite more than a fraction of the literature which has been accumulating for more than thirty years. Nor

can I discuss the results of those experiments in the field of embryology and genetics in which the interesting feature is the response of the organism rather than the means by which the results are obtained. The older literature also is referred to only occasionally, for it has been fully reviewed elsewhere (18, 63, 95, 110).

II

MORPHOLOGICAL AND PHYSIOLOGICAL EFFECTS

When a cell is exposed to X-rays or to radium radiations it quickly begins to show morphological and physiological changes, some of which can easily be seen, while others can be demonstrated only under favorable conditions. If we examine a cell during exposure, when it is still alive, we observe a series of events which lead to evident injury, a condition from which it may or may not recover, but we miss many details because they are invisible. By proper staining methods these can be brought out, but in the process others are lost to view. Both means of study are essential to a clear understanding of the effects produced by radiations.

The recent work of Nadson (70) on living yeast cells gives for the first time a clear picture of the progressive changes which begin almost as soon as the exposure commences and terminate in the death of the cell. His ingenious methods for radiating an individual cell warrant description. He fastens the radium salt, enclosed in an ebonite capsule from which the beta rays can escape, to an object lens. This is attached to the nosepiece of the microscope. Then with another lens he examines the field and selects some cell for study. Next he turns the nosepiece so that the radium is in position a few millimeters above the yeast. At the end of exposure he can examine the particular cell which he had previously selected, a necessary procedure in view of the wide variation in the response of different individuals even in the same pure culture.

The first visible effect consists in an increase in the number of fat droplets, which are normal constituents of the yeast cell. This change in the physical and perhaps chemical condition of the fats is not injurious if irradiation is not prolonged; such cells may grow and divide (36). Next, the protoplasm becomes turbid, due to the appearance of granules which are undoubtedly protein in nature. What has happened is that the colloidal protein has undergone a partial denaturing, that is, it has become insoluble. These changes are at first reversible, for the turbidity may disappear, in which case the cell recovers. Bordier (10) first described this phenomenon in proteins irradiated *in vitro*, and it has been demonstrated by others. Rajewsky (85), who studied the effect of ultra-violet rays on pure pseudoglobulin solutions, describes the appearance of the granules, which in his material were smaller than those which can be seen in yeast, and shows that they increase in number to a maximum, then nearly disappear, then reappear in smaller numbers, this rhythm being repeated several times within the course of a few hours. He compares this with the course of the erythema reaction in which there is a similar rhythm. With longer exposures the fat droplets do not seem to increase further but the number of protein particles does. The permeability of the cell membrane at first decreases, as shown by the Neutral Red test; while after long exposures it increases, and is accompanied by a coagulation of the protoplasm.

This investigation by Nadson constitutes an important contribution to our knowledge of radiation effects, for it

gives an insight into the first reactions of the living cell, a subject which has long been neglected.

In addition to these changes there may be seen in other kinds of cells an extensive vacuolization of the protoplasm (6) and a breaking up of the filamentous mitochondria into granules, a reversible reaction, since later they may resume their normal appearance. These changes can be seen more clearly in stained material in which, after severe irradiation, the mitochondria are found to be much altered in shape and in their arrangement in the cell. Probably some disappear entirely (109).

There is very little difference between these changes which follow irradiation and those which accompany degeneration induced by other means. The Lewises (61) find that when normal tissue culture cells are deprived of embryonic extract they eventually pass through a series of changes closely parallel to those which have just been described. First there is an accumulation of small granules in the cytoplasm which grow in size and number and take the Neutral Red stain. The mitochondria fragment and disappear in part. Before actual death occurs several irreversible changes can be seen. One is the disappearance of the degeneration granules and the growth of others which do not stain in Neutral Red.

It is not surprising that this sequence of events is the same in both cases. Protoplasm appears to react to all kinds of adverse conditions in the same way. That the histological changes are the same has already been mentioned. The observations just cited show that this principle holds true even in respect to the finer details of the degeneration process. Further study may reveal some of the changes which precede these and allow us to determine their nature more precisely.

In the living cell after irradiation the nucleus appears to be unchanged at first, even though the protoplasm gives clear evidence of being injured (51); but stained material shows that it is really profoundly modified. Such changes can be seen best when the cell is in mitosis. At such a time the chromosomes are found to be fragmented, or stuck together, or misshapen. At the metaphase some may fail to divide completely, the halves remaining attached by long chromatin bridges. After division the nuclei are often pyknotic. The asters and spindles are not affected unless the whole cell is severely injured, in which case they may fail to develop properly.

Although we can detect changes in one part of the cell before some other portion is altered, this is not proof that the one is more severely damaged than the other, nor can we judge the extent of the injury by the appearance of the cell at any particular moment. One that is to all appearances moribund may recover, while another that looks normal after exposure may die later.

When short, penetrating radiations are absorbed in a cell they quickly change the rhythm of mitosis. Even a brief exposure to gamma rays prevents those cells which were about to divide from beginning that process (14). Unless the irradiation is long continued or very intense they suffer no visible injury; indeed, they begin to divide soon after the exposure stops, giving no evidence that they have been permanently harmed. In tissue culture experiments, in which these phenomena can be seen to advantage, this temporary check in the onset of mitosis is followed by a very considerable increase in the number of dividing cells, the result being that the total number of divisions occurring within the space of a few hours after exposure is about normal (15). I have observed this in radiating Paramoecium, a

temporary fall in the division rate being often followed by an increase to a point well above that of the control. But the total number of divisions at the end of a few days is the same in both.

Cells which are already in mitosis when irradiation begins, complete the division on which they have entered; they are not checked (105). This is true even when the dose is so severe that it leads eventually to death (83). Richards (90) has found that Planorbis eggs, exposed during mitosis, are very materially accelerated for a brief time; and I have seen this also in the eggs of Arbacia (72). The result of this response is that immediately after exposure one may find in an actively growing tissue a large number of mitotic figures. But a little later none can be seen (88). This quiescent period lasts for a varying length of time, depending on the dosage, and is followed by a return of mitotic activity. Such divisions however are usually abnormal, but it is a curious fact that in a tissue which has been severely injured one may find perfectly normal division figures lying among many that are very aberrant. This I have seen many times in irradiated Drosophila eggs.

The absorption of radiant energy by the cell is followed by a number of reactions which undoubtedly have their origin in physical and chemical changes in the protoplasm. One of these is the alteration in the rate of protoplasmic streaming. In plant cells Williams (116, 117) finds that both X-rays and gamma rays increase the rate of flow at first, while longer exposures have the reverse effect. Zuelzer and Philipp (124), who describe an acceleration in streaming in many types of Protozoa, suggest that this is a result of a lowering of the viscosity.

Changes in viscosity are important signs of deep lying physiological changes which occur in cells in both normal and abnormal environments. For this reason a very considerable amount of work has been done to determine how the short radiations may affect the consistency of protoplasm. The results thus far have been conflicting. Fairbrother (30) observed a marked decrease after irradiation, amounting to 40 per cent of the original value; while Wels (113), who exposed serum and globulin solutions *in vitro*, found an increase. Weber (112) could see no change at all but felt that there may have been some. That the age or sensitivity of the cell may determine which reaction is to occur is suggested by Jannson (51), who finds that in adult leucocytes the protoplasm is liquified, while in immature myelocytes, which are more sensitive, it is coagulated. Finally, Nadson (70) shows that the viscosity may decrease at first and later increase. A theory which harmonizes these discordant results is offered by Lepeschkin (60). Changes in viscosity, he says, are produced by different agents which bring about a gradual decomposition of the principal compounds of protoplasm. When such decomposition occurs, the products "join in the dispersed phase of protoplasm and increase its viscosity. At the same time the removing of the lipoids from the dispersion medium may increase the disperse phase or decrease the viscosity of protoplasm. Both opposite changes of the viscosity may be produced by any injury effected, but its distinct decrease could evidently be observed only if the decomposition is not marked enough, while in the opposite case an increase of viscosity occurs."

It is probable that the permeability of the cell membrane is increased by both X-rays and gamma radiations, although several investigators have been unable to demonstrate it. Richards, for example, (91) exposed several kinds of marine eggs

and larvae to X-rays but found no evidence of an increase; and more recently Kovacs (58) has stated that toward serum albumen the cell membrane shows no increase after irradiation. On the other hand he demonstrates that the simpler proteins, dyes, and some other substances diffuse out more rapidly after exposure than before. This suggests that the effect is chiefly on the membrane itself. Kovacs believes that the result is due to the change in the electric charge of the ions at the surface. I have found (72) that the rate of penetration of ammonia into Paramoecium is noticeably quickened, especially by the slow beta rays, which are more likely to be absorbed at the membrane than are the more penetrating rays. The evidence, however, is not sufficient to warrant the statement that this region only is affected. More probably the change in permeability is a symptom of some general physiological change in which the entire cell is involved.

Whether short radiations act upon the lipoids of the cell is a much debated question. Some years ago Schwarz (98) declared that lecithin is changed to trimethylamin and that this substance is responsible for the injuries which develop after exposure. But this is very doubtful; sperm cells, which contain very little lecithin, are sensitive. Later Werner (115) stated that cholin is formed by the action of radiations on lipoids, and has a cytolytic effect. Neither of these views has been confirmed. But Nadson's observations show that the fats are in some way altered, a fact which assumes importance when we consider their rôle in the permeability of the cell membrane. What the precise relation may be between permeability and the radiated lipoid substances is still to seek.

Many divergent opinions are held regarding the effect of radiations on the hydrogen ion concentration of protoplasm. When irradiation is severe and the cells are injured, the pH turns to the acid side, as would be expected. Many proteins, irradiated *in vitro*, respond in the same way, but this is by no means a general rule. Karczag (54) believes that in the living cell the acidity tends to rise but that such a change cannot always be demonstrated because protoplasm has great powers of regulation, retaining its normal pH until it is severely injured.

That cells may recover from injuries produced by the radiations can easily be demonstrated, especially in the Protozoa, which are extremely resistant. Crowther (21) had to give Colpidium the huge dose of 80,000 Roentgen units in less than twenty minutes if he wished to kill the cells. If a smaller dose were given, or the same dose in a longer time, the cells gave every appearance of being moribund, but they recovered perfectly within a few hours and could be irradiated repeatedly on successive days without showing any permanent injury. Drosophila eggs also, though relatively sensitive (180 units kill half of a population of newly laid eggs) must be given a fairly intense dose within a limited time if they are all to be killed. Should the dose be light only a few eggs, that is, the most sensitive, will die, the others continuing to live even though the total dose is sufficient, if applied in a short time, to kill every one (75).

The environment of cells after irradiation is an important factor in determining whether they will or will not recover. Wood and Prime (123) found that tumor cells irradiated *in vitro* and inoculated at once into healthy animals, failed to grow; but if instead, they were put into plasma, they lived and multiplied.

There appears to be also a correlation between the rate of division after ex-

posure and the ability to recover. If Drosophila eggs are irradiated at ordinary temperatures and then divided into two portions, one of which is kept at 28° C. and the other at 17°, the latter will survive in a much larger proportion than the former (80). A similar result was reported by Strangeways and Fell (104), who worked with chick tissue cultures. The reason for the difference in behavior of the two lots was due, they think, to the lessened metabolism in the eggs kept in the cold. Whatever may be the explanation, the fact is clear that reparative processes go on more readily when cell division is checked.

What actually happens in the regeneration process is unknown. Evidently the initial changes in the protoplasm are reversible. The question is important, for the value of radiations in therapy and in biological experiments depends on the ability of some cells to recover from injury while others are destroyed.

III

THE LATENT PERIOD

The first changes which take place in an irradiated cell are so slight that they are invisible except under very favorable conditions. Only in fairly transparent, living cells which may be examined under high magnifications can the alteration in the physical state of the proteins and fats be detected; the acceleration or retard in the rate of cell division can be demonstrated only in tissue culture preparations or in dividing eggs. And unless the irradiation is intense or prolonged, the cells recover, giving no evidence of injury.

But even though cells eventually die in consequence of a severe irradiation, the first easily observed signs of injury make their appearance only after an appreciable time, developing gradually in a way analogous to the development of a photographic plate. This interval is called the Latent Period, a term used particularly by those who judge the effect of the rays by macroscopic signs. For example, the period for the human skin varies from a few days to two weeks, this being the interval between exposure and the first appearance of redness. The term is a convenient one, even though in one sense no latent period exists. What occurs between the time that the cell constituents begin to change under the influence of radiations and the time when the tissue shows very obvious injury is not known in any detail; but evidently the degeneration processes continue long after irradiation ceases.

The length of the latent period depends on a number of factors, of which one is the division rate of the cells. In the testis, for example, where this rate is high, the spermatogonia begin to show cytolytic degeneration about two hours after exposure (96), while injuries to the cutis may be many days in developing. To explain this condition Heinecke (41) suggested that the latent period ends when the irradiated cells die a natural death. That is, radiations affect only their reproductive capacity, the nutritive being unimpaired. If then a cell normally has a short life the visible effects on the tissue to which it belongs will quickly appear. The objection to this hypothesis is that some irradiated cells, especially eggs, begin to show injuries after many cell generations, as Hertwig and others have shown.

Another factor which determines the length of this period is the intensity of the dose. When great, the time elapsing before an extensive injury appears is short, and vice versa. Prime (82) exposed chick embryo heart tissue to the gamma rays from 100 mg. of radium and then planted it in serum. After a two-hour dose the cells pulsated and divided, but ceased by

the end of the second transfer. After a thirty-minute dose their activities ceased only at the time of the fifth subculture.

Oftentimes an irradiated organism will continue in an apparently normal condition until it undergoes some large morphological or physiological change, such as gastrulation, hatching from the egg, or metamorphosis. Thus Vintemberger (107) exposed one of the blastomeres of the frog embryo in the two cell stage, protecting the other by a lead screen. After a rather heavy dose of X-rays the embryo developed normally until the time of gastrulation when the irradiated half ceased from further growth while the remainder continued. When a small dose was applied, development was normal but retarded. So also, irradiated Drosophila larvae may continue to grow until the time of pupation or the emergence of the imago.

The reasons for the gradual development of injury are not clear. Of the theories advanced to explain the phenomenon many are based on the reactions of large organisms, in which the secondary effects of irradiation occupy a large part in the clinical picture. Others based on the reactions of cells seem to come closer to being working hypotheses. Schwarz (99) suggests that the degeneration of proteins is the essential factor. In such a change, these become what he calls "actinoproteins," which are poisonous, although the toxic effect is not great. Later, by further transformations they become more and more toxic and their action on protoplasm produces degeneration products which are inflammatory. The basis of this hypothesis is the well known fact that after irradiation there may be a slight response, often an acceleration, which is followed by apparent recovery and then by more extensive injury. This is characteristic of the erythema reaction; it can also be demonstrated in dividing eggs. The first response is due to the actinoproteins directly; the second, to the derived products which are gradually formed and hence exert their effect some time after exposure. These products are called "necrohormones" by Caspari (16). When they have killed the cells which produce them they are supposed to escape into the body and to bring about a general reaction.

Flaskamp (32) introduces another idea. The degeneration products, whose nature he does not discuss, stimulate the production of antitoxins. If the dose is weak, these are sufficient to overcome the toxic effects, and no damage results. But if the dose is strong they are not adequate, and injury appears. The latent period is the time during which these two antagonistic forces are at war and before the toxic substances have gained the victory. One merit of this hypothesis is that it takes into account the tendency of a cell to recover from injury. This is a general biological phenomenon which is usually neglected by those who form theories to fit particular cases. But if Flaskamp's idea is true we must believe that antitoxins are less effective, or produced in smaller quantities during the anaphase of mitosis than during the resting period.

These are little more than formal explanations of the problem; the agents which produce the end results are really unknown. Some observations by Knipping and Kowitz (56) indicate that after irradiation of an entire organism the proportion of globulins in the serum is increased, while that of albumen is decreased. The clinical effect of the treatment resembles that which follows the injection of foreign proteins. This does not prove, however, that the two phenomena are related.

IV

SENSITIVITY

That different kinds of cells and tissues vary in sensitivity was observed very soon after the discovery of X-rays in 1895. The first workers, who naturally did not realize the danger connected with their experiments, found that the skin is susceptible, a moderate exposure producing a slight burn or erythema which appears some days later. This skin reaction soon became a measure of dosage, and it is still widely used although by no means satisfactory. The output of the first tubes was highly variable and the early investigators determined the intensity of the beam by observing the shadow cast by the bones of their hands on a screen. While these brief exposures produced no burns, their cumulative effect was very serious, many workers losing their lives years later as a result. Among these martyrs to science was Bergonie, who before his death in 1925 made contributions of greatest value to radiology.

Further studies make possible the arrangement of the different mammalian tissues in the order of their sensitiveness. In such a list (92) the germinal epithelium and blood forming organs stand at the top, while at the bottom, being least susceptible, are the liver, and nerve and fat tissue. A fixed order is not possible, for some tissues, such as the skin, vary in sensitiveness with the age of the individual, being highly susceptible in young children and comparatively resistant in the aged. Health and disease are also controlling factors in determining the reaction to radiations.

There is a striking difference in sensitivity between different types of cells in the same organ. The most familiar example is the testis, in which the sperms, in their stages of development, show marked variations in response. The first spermatocytes are usually regarded as more susceptible than the spermatogonia or the fully formed sperms. So also, the lining of the blood vessels is more easily injured by radiations than the surrounding muscular coats.

During the division cycle, cells show marked variations in sensitivity. A dose applied during the resting stage may produce no visible injury, but if given during actual mitosis, may be lethal. And the effect is much greater at some stages of division than at others, although just what stage is most sensitive has not been agreed upon. Strangeways and Hopwood (105) observed that cells already in division continue to divide if irradiated not too severely, while those that are ready to start the process are inhibited for the time being. From this they conclude that just before the prophase the cell is more sensitive than at any other time. Mottram's early experiments (67) indicated that the metaphase is the moment of least resistance, and this view has found wide acceptance. Regaud (87) finds that during the prophase and anaphase sensitivity is at its height, while Vintemberger (106) in a recent publication states that the telophase is the critical time. He exposed frog eggs to brief but intense radiation during the periods which experience had shown were occupied by the various division stages. After exposure the eggs are allowed to develop, the criterion of effect being the percentage of embryos dying. He found that susceptibility rises from the prophase to the telophase and then falls abruptly when division is completed.

In view of Richards' observation (90) that dividing eggs, when exposed, hurry quickly through the mitosis which is in progress, it is difficult to say how long a single stage may continue. If it is nor-

mally very short, as is, for example, the metaphase, the actual time the cell can be exposed in such a stage may be so short that ordinary irradiation may not affect it at all. The question of the most susceptible stage in mitosis can best be settled by observations on living cells in which the changes following irradiation can be watched in the order of their appearance.

Even more debated is the question of the most susceptible part of the cell, a problem rendered difficult because of the different criteria by which the effect of radiations is estimated. That the nucleus is highly sensitive has been demonstrated in many ways. The long series of experiments by Hertwig and his students (42, 43) showed that the beta and gamma rays of radium can injure the sperm or egg nucleus without destroying either cell's activity in the fertilization process. An irradiated sperm is motile and can initiate development in a normal egg. If it has been slightly irradiated it interferes with mitosis, the eggs soon dying. But if it is severely injured it plays no part in subsequent development, which is fairly normal. The nuclei in the growing embryo are haploid. Here then is a seeming paradox in that a slightly injured sperm causes more disturbance in development than a severely injured sperm.

Dalcq (24) has recently repeated these experiments on the frog egg, using X-rays, radium, and ultraviolet light. When the sperm are exposed to the latter and then added to normal eggs the paradoxical effect is very evident; when X-rays or radium are employed it appears only occasionally.

In the irradiated egg of Chaetopterus (73) the nucleus may be so injured that it can take no part in the first cleavage division after a normal sperm has entered. The protoplasm of such an egg is not, however, permanently injured. The egg membrane lifts off, and the sperm is drawn in just as in normal eggs. The normal nucleus plays no part in the development which ensues, cleavage taking place under the influence of the sperm nucleus alone. Another experiment (108), mentioned because of the ingenious method used, again demonstrates the susceptibility of the nucleus. Frog eggs are irradiated through small holes in a lead plate, the holes being so spaced that the rays passing through them strike the nuclei of the blastomeres in the two cell stage. Eggs thus treated die, but are seemingly uninjured if the narrow pencils of rays are allowed to strike only the protoplasm. No further proof is needed to show that chromatin is a highly susceptible part of the cell.

More delicate effects of radiations on the nucleus have recently received much attention. When Drosophila is irradiated the nuclear mechanism may be so altered that the rate of crossing over during the synaptic period is modified (65). The work of Muller (68, 69) and others shows in addition that out of the entire chromosome complex a single gene may be modified, the change being demonstrated by genetic tests. Cytological proof of visible malformations in the chromosomes is furnished by Dobzhansky (28), who shows that irradiation may result in the breaking of one or more of the chromosomes into fragments of varying proportions. Of great interest is the fact that the actual size of the fragments is roughly proportional to their size as determined genetically. Radiations have proved a useful means of inducing a rapid mutation rate and of disarranging the mechanism of heredity. The genetic results of such experiments are of greatest interest, but since they lie beyond the scope of this review, they can only be mentioned.

From this evidence one might conclude that radiations produce injuries in the chromatin alone. This is not necessarily true. The cell is a unit, and whatever affects one part must affect the rest also. But it may be that the cytoplasm has a greater regulative power than the nucleus and hence can recover from an injury. Needless to say, any cell or any part of the cell, no matter how resistant, may be destroyed by radiations if the dose is strong enough.

In general, rapidly growing tissues are highly susceptible. So also are cells in which differentiation is not great. For example, the undifferentiated formative cells of Planaria can be practically destroyed by radiations although the animal itself continues to live for some time (22). The developing eggs of Drosophila are easily killed by small doses of X-rays; the larvae are more resistant; the pupae, still more so, while the adults succumb only to very large doses (66). Bergonie and Tribondeau (4) summarized their conclusions regarding the reaction of cells to radiations in the statement that sensitivity varies directly with the reproductive capacity of the cell and inversely with its degree of differentiation. This principle is true in general, although there are many exceptions. A rapidly growing melanosarcoma is highly resistant, while an inactive basal cell sarcoma on a similar site is very responsive.

When we seek a reason for these differences in sensitivity among different kinds of cells, and in the same cell at different periods of its division cycle, we are faced with two difficulties neither of which can be overcome at present. One is that we know little of the nature of the changes which radiations produce, and the other, that we are still ignorant of the nature of the normal functions of the cell which the radiations disturb. It is not surprising therefore that we cannot form any general hypothesis which will explain all of the various results which have been obtained.

The suggestion has often been put forward that sensitivity is dependent on the metabolic rate of the radiated cells. Dormant seeds, in which respiration is at a low ebb, are resistant, but when they germinate, their susceptibility rises with the rate of respiration (57). The rate of oxygen consumption in normal and pathological tissues is said to vary directly with their sensitivity (35). Instances of this kind could be multiplied. But there are important exceptions. For example, the metabolically active cells of the liver are highly resistant; and the eggs of Ascaris, radiated under anaerobic conditions when their metabolism is much reduced, are only a little less sensitive than when they are radiated in air (45). Furthermore, there is no apparent relation between the variations in susceptibility during mitosis and the metabolic rate. The experiments of Rogers and Cole (93) show that during cleavage, heat production is constant; and Shearer (101) found that the rate of oxygen consumption and CO_2 production is steady, not showing fluctuations during the stages of mitosis. These instances, however, are not sufficient to outweigh the large amount of evidence which indicates that there is some connection between susceptibility and the metabolic rate, or some physiological condition closely bound up with it.

Another hypothesis to account for sensitivity to radiations is based on the degree of hydration of the protoplasm. Schaudinn, in 1899 (94) first pointed out the fact that those Protozoa whose protoplasm is most fluid are also most susceptible. Petry (81) also has shown that seeds are more sensitive when swollen with water, while they become resistant if allowed to dry a little. In this connec-

tion it should be recalled that in young and active cells, such as are found in growing root tips of plants, the protoplasm is much more fluid than it is in adult cells. During cell division the viscosity of protoplasm undergoes striking changes, rising abruptly during the prophase, falling sharply at the metaphase and then rising again gradually (40). The precise relation between the various stages of mitosis and protoplasmic viscosity is not wholly clear, but the phenomena are of interest because they appear to run more or less parallel with the changes in susceptibility to radiations, and they are the only phenomena thus far known which show this relation. According to Heilbrunn (40) "the periodic cycle of rhythmic changes in viscosity of dividing cells is almost certainly related to the rhythmic changes in susceptibility of dividing cells to various toxic substances."

Some attempts have been made to correlate the degree of sensitiveness with the amount of radiant energy which the cell absorbs. The higher sensitivity of the nucleus was explained by the fact that in this cell organ there is a higher concentration of phosphorus which, because of its atomic weight absorbs more energy than carbon, oxygen, or hydrogen. But actually no such correlation exists. Red blood cells with their high iron content are less sensitive than the lymphocytes, which contain very little iron. And experiments show that the amount of radiant energy absorbed by blood, muscle, fat, Locke's solution, and pure water, are practically identical. That is, the differences, if they exist, are too small to be measured with the apparatus at our command. We must believe therefore that the same amount of energy is absorbed by all kinds of cells. The different quantitative effects may be due to the chemical make up of the cells, or to the relative stability of the compounds, or to differences in regenerative power. But these are only guesses; there are at present few data on which they are based.

The question of sensitivity is the chief problem before the radiologist, for all work with radiations depends on the fact that in the tissues or cells under exposure some part will respond more quickly than another. This is the basis of radiotherapy and of those genetic experiments in which the chromatin or even some minute portion of it is altered while the remainder of the organism is not permanently changed. The problem is still unsolved. As Holthusen remarks, "The radiosensitivity of cells is closely bound up with their chemical structure and with their organisation, yet we do not know what those substances are which are responsible for the great differences in susceptibility." (48).

V

STIMULATION

A question which has been much debated by students of radiology is whether cell activities can be promoted by very light doses of radiations. The belief that this may be possible is based on the Arndt-Schulz law, which states that many agents, when applied in small doses, bring about an acceleration; in medium doses, a depression, and in large doses, a complete stopping of vital actions. This principle was for a time widely accepted by radiotherapists, who explained the occasional rapid growth of tumors after radiation by saying that the dose had been too weak. Such an explanation is hardly logical, for the law is of limited application; indeed, it is not a law at all, but only a generalization whose value is doubtful.

Those who have found evidence of acceleration have used the word "stimula-

tion" to describe the phenomenon. The term is unfortunate, for in its proper sense it means any change in the state of the organism, whether excitation or depression. But the latter meaning has been disregarded; stimulation in radiological literature refers to an acceleration in the rate of growth or to an increase in functional activity. Usually it implies a reaction favorable to the organism, although sometimes it is used to refer to any quickening in the normal tempo of vital activities, even though the end result is an obvious injury. I shall use it in the former sense in this discussion.

A large amount of the experimental work carried on to determine whether or not radiations can promote growth has been done on plants, especially young seedlings. Many investigators find that the rate of growth of the roots or shoots is accelerated by weak doses, or that the radiated plants have stronger stems and heavier leaves than the controls (52, 38, 50). Their conclusions, however, are open to criticism because they are based on measurements of very few individuals; the factor of normal variability is practically neglected. Jüngling, for example, believes that half a dozen seeds are sufficient for a single test, with one or two for controls. Those who have repeated these experiments using very large numbers of specimens are outspoken in their belief that no stimulation occurs (100, 2). Not uncommonly a group of lightly radiated seeds may be found to grow faster than the controls, but such isolated cases are not significant. On the other hand, Arntzen and Krebs (3), whose technique was excellent, found a slight but real acceleration in the growth of peas during the first two days after irradiation. This was followed by a retardation in every case.

When the shoots of various plants are lightly irradiated in the proper stage of development their buds open sooner than do those of the controls. Weber (111) suggests that the acceleration may be due to a change in permeability or to increased oxidation. Reiss (89), however, believes that there is no evidence of real stimulation, that is, of quickened normal growth, for he finds no increase in the number of mitoses in the irradiated material. On the contrary, the cells are clearly injured as shown by the shrunken protoplasm and the peripheral position of the nuclei. Furthermore, they are decidedly larger than those of the control plants. Such an increase is common in irradiated cells. Nadson (70) believes that it is due to increased cell turgor. It cannot be regarded as an evidence of healthy growth but rather of injury. The most enthusiastic believer in the stimulating action of radiations is Stoklasa (103), who states that "in weak concentrations, emanation affects favorably mitosis, plant development in general, the interchange of gases, the activity of chlorophyll, and of flowering and reproduction." Some doubt is thrown on his statements by the fact that the doses which he found large enough to produce a retardation were much smaller than those which Falta and Schwarz (31) report as stimulating. The results have not been confirmed.

Many experiments show that weak radiations may accelerate the rate of mitosis and of growth in animal cells. In most cases this reaction is short lived, or terminates in an obvious injury. Among the first to describe the quickening effect were Lazarus-Barlow and Beckton (59), who treated Ascaris eggs with very minute quantities of radium. Those eggs that were exposed for long periods at low temperatures were found to be in the two-cell stage while the controls were still uncleft. From this they conclude that under the

influence of these radiations "cellular division proceeds at an accelerated rate." The observations did not extend beyond the two-cell stage. I have observed also that the first division of Arbacia eggs may be slightly accelerated, but the effect seems to disappear very soon (72). Richards (90) reports the same results on Planorbis. Obvious injury, however, appeared during later development. Hoffmann (44) found that when frog eggs are lightly irradiated they often develop more rapidly than the controls. He is careful to state that stimulation can be demonstrated only if one is lucky; that is, the internal and external conditions of the eggs must favor quickened growth.

The experiments of Markowits (64) on Paramoecium are widely cited as giving evidence of stimulation. But his methods were such as to throw some doubt on the value of his conclusions. He made no daily isolations of the descendants of the irradiated cells, nor did he determine the division rate, but only counted the number of individuals alive on the tenth day after exposure. His data show that the irradiated cell, in one test, had divided ten times while the control had divided but seven times. This low score for the control indicates that the culture medium was faulty.

There are some experiments which show that the rate of cell division may be definitely accelerated and that this condition may continue for some time. Of these the most striking are those of Nasset and Kofoid (71), who exposed mass cultures of *Endamoeba dysenteriae* to radium. In one test in which the exposure continued for eight days, the number of cells at the end of the third day of irradiation was about five times as great as in the controls. Four days after the removal of the plaque there was a great reduction in the population. The cells showed characteristic injuries,—abnormally large size, vacuolization of the protoplasm, atypical nuclei and mitoses. Cells which were not severely injured apparently recovered, for the irradiated cultures could be kept alive by transplantation.

In a few instances true stimulation seems to occur; that is, the quickened tempo of growth is not followed by any observable abnormality. Hastings, Beckton, and Wedd (39) exposed silk worms in various stages of development. When eggs are treated they hatch out earlier than do the controls; if the larvae are irradiated the cocoons are heavier than normal. In these experiments the number of individuals treated was adequate and the tests were repeated in successive years. Similar results are reported by Blumenthal and Williams (8), who used grasshopper eggs, treating them with X-rays and with radium. But these observations, standing alone among the large amount of negative evidence, are not sufficient to warrant the conclusion that true stimulation of growth follows exposure to weak doses of radiations.

The same statement may be made in regard to the experiments on the effect of the radiations on cell functions. Stephan (102) draws a sharp distinction between growth stimulus, which he denies, and functional stimulus, which, he believes, can be demonstrated. He finds that the activities of the kidney, spleen, and thyroid are augmented after mild doses. But Czepa (23) in a careful review of the entire question of stimulation shows that the functional increase, which is an undoubted fact, follows in every instance a destruction of the more susceptible cells in the radiated region. It is therefore a response to the action of degenerating cell products rather than a direct stimulation by the rays.

Some work has been done on the effect

of radiations on the respiratory rate. In many cases this appears to be increased, but whether this result is normal or pathological is not certain. Blumenthal and Williams (8) have made quantitative measurements on the rate of oxygen consumption in radiated grasshopper eggs and find a definite acceleration. The higher rate becomes noticeable five days after exposure. This is a very long latent period, considering the fact that the eggs were dividing rapidly. Kimura (55), who studied the CO_2 output of radiated tumor cells, exposed *in vitro*, found an increase which was not always associated with the rate of mitosis. That there may be no relation between the rate of CO_2 production and growth is the conclusion of Redfield and Bright (86). Their irradiated seeds, from which CO_2 was given off more rapidly than from the controls, were obviously injured, some not germinating at all. On the other hand, Bersa (5) reports a decreased respiratory rate in irradiated beans, while Wels (114) is unable to demonstrate any change whatever in muscle cells, in yeast or in bacteria.

The many experiments in which entire animals are exposed to radiations show that the respiratory rate is lowered. Such results are difficult to interpret, for when all of the organs of a large animal are irradiated each responds in its own way, depending on its sensitivity at the moment. The CO_2 output is thus an average of the activities of many parts. While this is of clinical interest, it does not throw light on the action of the rays on single cells.

The evidence now at hand points to the conclusion that radiations do not directly stimulate normal activities of the cell; their primary effect is always an injury from which the cell may recover perfectly. But the degeneration products which arise after irradiation may temporarily quicken the tempo of some normal processes, such as protoplasmic streaming and mitosis; an acceleration which is followed by a retardation and often by very obvious injury. Such reaction is secondary, and is not true stimulation in the sense in which the term is used in radiological literature.

VI

PHYSICAL THEORIES OF THE ACTION OF RADIATIONS

A theory to explain the way in which radiant energy produces changes in a living cell must be based on certain physical assumptions regarding the nature of this energy and of the atoms and molecules which it affects. In the discussion which follows I have included only those assumptions on which the biological theories are based, and have purposely omitted all other matter.

There are two ways in which we may picture a beam of radiant energy, whether it be of visible or ultraviolet light, X-rays or gamma rays of radium. We may regard it as consisting of electro-magnetic vibrations, or we may picture it as made up of discrete bundles of energy or quanta, which are shot like bullets from their source. Both conceptions seem to be necessary at present, for there are many phenomena which can most readily be explained by one or the other but not by both. The first prevails when we describe the quality of the beam in terms of wave length. Short rays, like the gamma rays of radium or those produced by an X-ray tube running at high voltages, have waves ranging from 0.01 to 0.1 Angstrom units in length. (This unit is 1×10^{-8} cm.) Soft rays produced by special tubes at potentials of 10 KV. or less are relatively long, that is, more than 1.5 Angstrom units. They are thus more than 200 times as long as the shortest waves. Although the actual difference between the extremes is very

small, being one or two ten millionths of a millimeter, their penetrating powers are very different. The shortest can pass through thick sheets of lead, while the longest are absorbed in a few millimeters of tissue. Since this conception of energy in the form of waves is convenient and sanctioned by long usage, it is employed, even by those who believe that energy is actually transmitted in another form.

The second view, which regards the beam as a procession of rapidly moving bundles of energy, prevails in the theories which have been formulated to explain the physical and chemical changes which can be demonstrated in living cells. Quanta differ from each other in their energy content, for this depends on their vibration frequency (the reciprocal of the wave-length), which for gamma rays is very great, while for light waves it is very small. The proportion between the two is of the order of half a million to one. When they strike the atoms of protoplasm they give up some or all of their energy, and it is this transformed energy which initiates the physical and chemical changes.

To understand how this transformation takes place we must picture the atom as made up of a nucleus around which are rotating at enormous velocities a number of negatively charged electrons, some in orbits close to the nucleus and others at greater distances. The former are closely bound and can be dislodged only by a large expenditure of energy such as is found in a quantum of X-rays; the latter, being loosely held, are easily displaced by the small quanta comprising light rays.

Now when a beam of X- or gamma rays strikes a substance composed of such planetary systems, the quanta may chance to pass clean through it without colliding with anything, and emerge on the further side having lost no momentum. Such quanta have no effect and are therefore without biological interest. But others suffer collisions. When one strikes an inner electron it may knock it from its course to another orbit at a greater distance from the nucleus. In doing this the quantum may give up all of its energy, in which case it ceases to exist. But when such a displacement occurs the atom as a whole acquires energy, for the negative electron can be held by a smaller amount of energy than before. At such a time the atom has a high reactive ability and can enter into chemical combinations which were impossible before. It is in an "excited" condition which lasts for a brief instant, perhaps less than a millionth of a second, for the attractive force of the nucleus is enough to pull the electron back into place. This is the first step in the photochemical process.

The X- and gamma ray quanta possess enough energy to displace an electron from the inner orbit; they may also separate it completely from its atom and send it flying off into surrounding space. This electron is in reality a beta ray since, like the beta rays of radium, it is a negatively charged particle. It is also a cathode ray. Wilson (118) has photographed these photoelectrons, or rather, the water vapor which condenses on them, and shows that the X-ray beam itself is invisible; its presence can be detected only by the ionization which it produces.

The number of these primary beta rays is not large in comparison with the total number of electrons in the substance traversed by the beam, but they produce indirectly a very considerable effect. Each one, while traveling at high speed, may knock off other electrons or displace them before it comes to rest, so that actually it produces a large amount of ionization. "The absorption of one quantum of 160 KV X-ray is much like a highly localized burst of ionic shrapnel, in which

about 4000 ion pairs are liberated in less than a millionth of a cubic centimeter." (20) These secondary electrons travel but a short distance and give up their energy in the cell in which they arise.

In this discussion the quantum has been represented as giving up all of its energy at the moment of collision when it sets free a photoelectron. But this does not always occur. A quantum of hard X-ray may strike an electron, displace it, and still retain a considerable portion of its momentum. Because of the collision its course may be changed; it may be scattered through any angle. Most of the quanta continue forward, some are thrown to one side, and some return in the direction from which they have come. Such scattered quanta now collide again and again with electrons, each time setting one free or displacing it, until they have so little energy left that they cannot affect even the electrons of the outer ring. This phenomenon was first investigated by Compton (19), who measured the loss in frequency, or in the other terminology, the increase in wave-length of the deflected rays. The amount of increase varies with the angle of scattering, being greatest at 180°. Biologically these rays, especially those scattered through wide angles, are of greatest importance, for they increase the effectiveness of the beam by as much as 40 per cent if the area and volume of the scattering medium is large. From X-rays produced at low voltages the back scatter is not great; nor is it from very hard X-rays. In this case most of the rays are scattered forward (78).

Radiation quanta produce effects only when their energy is absorbed, that is, when it is imparted to the electrons in the absorbing substance. The amount of ionization produced by a beam of definite hardness is the same for all tissues, and this is parallel to the amount produced in air by the same beam. For this reason the amount of air ionization is taken as a measure of the ionization which occurs in tissues under the same conditions. This can be measured by appropriate apparatus.

These are some of the elementary principles on which the theories of the action of short radiations on protoplasm are based. Briefly, the change in the molecules of living matter is produced by the displacement or removal of electrons under the impact of energy quanta. This results in a disturbance of the electrical balance, that is, an "excited" condition in which chemical transformations may occur. This is the first step. The second is taken when the excited molecule or atom collides with another. The result of this event may be a molecular breakdown, a process which perhaps is the first of a series of changes which terminate in a very considerable chemical transformation. What these chemical changes are is still unknown.

One theory which is based on these physical assumptions is the Point Heat hypothesis, put forward by Dessauer (26). In their opinion, the major part of the energy absorbed by tissue is transformed into heat. That is, when an excited molecule meets an inactivated one, the displaced electron returns to its original orbit and the energy which is given off in the process is imparted to the colliding molecule in the form of movement. Thus heat is generated and there is a rise in temperature at the point of collison. Dessauer has calculated that the protoplasm in the immediate vicinity may attain a temperature of 100°C., a point well above the coagulating temperature. As a result, many minute areas of dead matter are formed, and these, when decomposing, set free poisonous substances which produce typical X-ray injuries.

Holthusen (47) criticizes this idea on

the ground that while heat is undoubtedly developed, the amount is actually too small to have any biological effect. By experiment he determined the length of exposure to a high temperature necessary to produce in Ascaris eggs the same amount of injury that a dose of 600 Roentgen units produces. The heat energy was so much in excess of what the X-rays could possibly generate that he concludes that the theory is untenable. Holthusen himself believes that the chief effect of the rays is due to the molecular decomposition produced by the secondary electrons.

Another hypothesis is based on the behavior of the colloids when their electrical charges are altered by the displacement of negative electrons. In colloidal solutions there is a difference of potential between the particles and the fluid in which they are suspended. When this is disturbed the particles are precipitated (10). Schinz (95), in a general review of X-ray problems, objects to this on the ground that while such precipitation actually can be seen *in vitro* the doses necessary to produce it are so large that it could not occur under therapeutic conditions. But in the living cell such changes can take place more readily than in a test tube. In all probability this change in the electrical balance is not the only reason for the change in the state of the colloids; they are undoubtedly altered in other ways, although at present this has not been demonstrated.

A change in the electric charge may also serve to alter other physico-chemical conditions of the cell, such as the viscosity, the surface tension, the hydrogen ion concentration, etc. (53). How far these hypotheses may serve to explain the biological effects of radiations remains to be seen. But they are an advance over the older theories in that they are based on a physical foundation.

VII

APPLICATION OF PHYSICAL THEORY TO BIOLOGICAL PROBLEMS

The quantum theory has very recently been employed by physicists to explain the wide variation in response to radiations in a population which is supposedly homogeneous. This variation is familiar to those who have observed the action of injurious agents of various kinds on cells and organisms. If the percentage of individuals that survive be plotted against the length of exposure to some agent the points will fall along an S-shaped curve, whose course is characteristic for each kind of organism. Four examples are given in Figure 1. That of Ascaris eggs (125) is practically symmetrical; the Drosophila egg curve differs from it in that the lower portion is much less steep (79). This means that after prolonged doses there is still a considerable proportion of eggs that remains alive. The curve for the protozoan Colpidium (21) shows that a long exposure must be given before any cell dies; then the death rate rises rather suddenly, as shown by the steepness of the slope. The carcinoma curve has the same general characteristics but differs in some respects from the others (120). The data were obtained in experiments with finely minced tumor tissue which was first radiated and then inoculated into healthy animals. The curve thus shows what proportion of tumor cells survived the radiation and commenced to grow in the host animal. Each of these four curves is distinct from the others and cannot be confused with them.

When the data on which such curves are based are plotted on logarithmic probability paper they tend to lie along straight lines as shown in figure 2. In this paper "the ordinates are so spaced

that any set of figures which follow the natural law of probability will plot out, not as an ogee curve, but as a straight line" (11). Obviously not all organisms

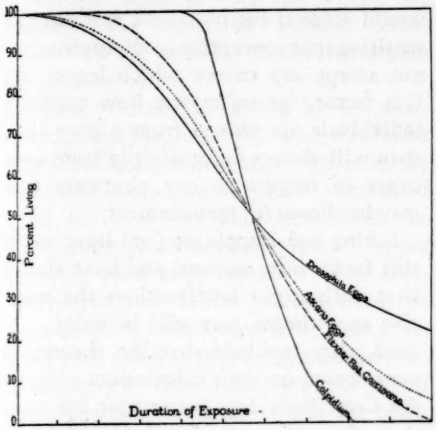

FIG. 1. TYPICAL CURVES SHOWING THE PERCENTAGE OF INDIVIDUALS SURVIVING AFTER EXPOSURE TO RADIATIONS

follow this law perfectly—that is, the frequency distribution of whatever character is being measured is not necessarily symmetrical. But an inspection of the curves given in the figure strongly suggests that it is true in these cases.

Biologists have usually assumed that such curves represent the normal variability in sensitiveness of the individuals to an injurious agent. That is, some are highly susceptible, some are highly resistant, while the majority show medium sensitiveness. But physicists have proposed a very different explanation. Blau and Altenburger (7) assume that there is no biological variability—that every cell or organism in a homogeneous population is like every other in sensitiveness, and that each dies when it has absorbed a sufficient number of X-ray quanta. If all should absorb this number at the same moment, all would die simultaneously. But, since they do not, the probability is that some may chance to be hit the requisite number of times sooner than others. Thus when a large number of individuals, such as Protozoa, Drosophila eggs, or tumor cells are radiated, some die quickly because they have happened to receive the lethal dose soon after exposure begins, while a few others happen to escape for a long time.

Somewhat later, Crowther (21) advanced substantially the same theory and developed it much further. The biological data on which he based his argument he obtained from experiments with Colpidium. He states that the course of the mortality curve is to be expected if the cells are killed by a definite number of quantum hits, assuming that the probability of a hit occurring remains constant throughout the exposure. Now a hit must be made, according to his theory, on a small sensitive spot of protoplasm whose nature is such that when it is sufficiently damaged, the cell dies. What this spot may be he does not attempt to determine,

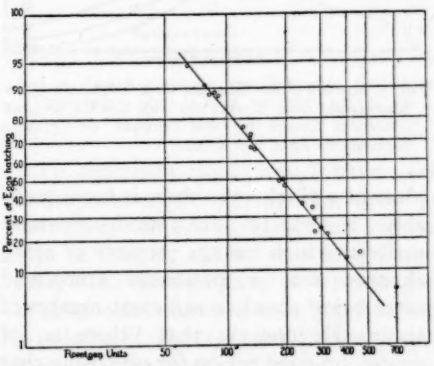

FIG. 2. THE SURVIVAL CURVE OF DROSOPHILA EGGS PLOTTED ON LOGARITHMIC PROBABILITY PAPER

but according to his calculations, it is about the size of a nucleus. Assuming this size, he finds that for Colpidium, 49 hits must take effect before death occurs.

Now the chance that the sensitive spot will receive this large number of hits in a brief exposure is very small; in other words, no cells die at first, as the curve shows. But after a time most of them will have received, say 40 to 45 hits. Thereafter the chances of receiving the lethal number are great: the cells therefore die at a rapid rate. But a few escape entirely unless the exposure is very intense.

Clark (17) criticizes this application of the quantum theory, showing that in

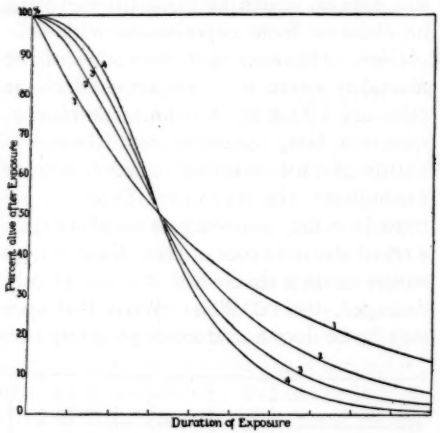

FIG. 3. ILLUSTRATING CONDON AND TERRILL'S VIEW REGARDING THE EFFECT ON THE COURSE OF THE SURVIVAL CURVE OF THE NUMBER OF QUANTA NEEDED TO KILL THE CELL

place of a single spot there is more probably a widely distributed sensitive material which has the property of being changed into a poisonous compound after being struck a sufficient number of times. He remarks that "there is, of course, no good reason for supposing that it is the true explanation of the phenomenon." That is, he recognizes that this type of theory is a formal explanation which does not take into account all of the facts known to radiologists.

The theory is based on the assumption that all cells are alike in sensitiveness. Crowther, however, states that if they should show variability in this respect, the shape of the survival curve would be the same; that is, the fact of variability would account for its course and not the sensitive spot conception. Biologists cannot accept any theory which leaves out this factor, for no matter how carefully individuals are chosen from a pure line, they will always differ slightly from each other in respect to any character that may be chosen for measurement.

Schinz and Zuppinger (97) have taken this factor into account, and have shown that with slight modifications the sensitive spot theory may still be valid. Indeed, they conclude that the theoretical curve based on their calculations actually fits Crowther's data better than his own. A further step was taken by Condon and Terrill (20), who discuss the consequences which should follow when cells are killed by quanta of different sizes, that is by X-ray beams produced at different voltages. They show that if one large quantum, produced at 190 KV., is sufficient to kill a cell, the mortality curve should have one shape, while if smaller quanta, produced at 100 KV. are employed, more than one will be necessary to bring about the same result, and in such a case, the curve should have a different shape. The results of their calculations are shown in Figure 3. The curves have been drawn so that the abscissas for 50 per cent death coincide. The curve which should result when death is due to one quantum hit slopes steeply down from its point of origin and then turns toward the horizontal; the curve for four quantum hits is at first nearly horizontal, then very steep, and finally almost horizontal.

Experimental evidence which supports this view is given by Holweck and Lacassagne (49), who exposed bacterial cul-

tures to very soft X-rays, the wave lengths being 4.0 and 8.0 Angstrom units. According to their calculations, if one quantum hit of the shorter rays is effective, then four hits of the longer are needed. The sensitive volume corresponds to the volume of the chromatin in ordinary cells.

More evidence is offered by Glocker, Hayer, and Jüngling (37), who irradiated the horse bean, *Vicia faba*, with carefully measured doses of soft (80KV.) and hard (180 KV.) X-rays and determined the percentage of individuals which stopped growing soon after exposure. The courses of the two curves plotted from the data obtained in this way, differ somewhat from each other, a proof, according to the authors, of the differential effect of small and large quanta. When the beans were placed on a large wooden block from which there was a considerable amount of back scatter, the death-rates were much higher than before, because of the additional energy furnished by the recoil electrons. In this experiment the courses of the two curves are nearly alike, and practically the same as one of the preceding curves. Such a result causes one to doubt whether there is any real difference in the curves.

In summary, the theory which has just been outlined rests on the assumption that X-rays produce their effect by means of discrete quantum hits in a sensitive region. The number of hits required depends, aside from the nature of the cell, whether sensitive or resistant, on the size of the quanta. And on this number depends the course of the mortality curve.

In the present state of our knowledge we cannot prove or disprove these assumptions. There can be no question but that cells are killed when they have absorbed a sufficient amount of energy which is given up by the quanta; but whether only that energy which is absorbed in a definite region such as the nucleus is effective in causing the death of the cell seems very questionable. So close are the interrelations between the nucleus and cytoplasm that we cannot say that injuries to the latter are wholly distinct from injuries to the former. The conclusion of the argument, that the mortality curves should vary with the wave-length, that is, the quantum size, can be put to a practical test.

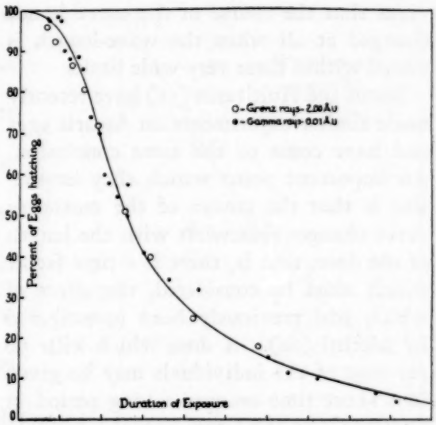

FIG. 4. THE COURSE OF THE SURVIVAL CURVE OF DROSOPHILA EGGS IS NOT AFFECTED BY THE WAVE LENGTH, I.E. QUANTUM SIZE, OF THE RADIATION

To determine this point I have used Drosophila eggs (75), exposing them to very short waves of highly filtered gamma rays of radium, and to very long Grenz rays. The former have a wave-length of about 0.01 Angstrom units, representing a voltage of about 1000 KV; the latter have a wave-length of about 1.7 units and are produced at 10 KV. Inasmuch as the quantum size varies with the square of the voltage it is obvious that if size makes a difference in death-rate, it should be very apparent in this test. The results are shown in Figure 4. The data

have been brought together so that the abscissas for 50 per cent killed are the same. The small solid circles show the results of individual tests with gamma rays; the large open circles represent averages of several experiments made with Grenz rays under uniform conditions. The solid curve itself is based on data obtained from numerous experiments with X-rays involving more than 200,000 eggs, made during the past four years. In these the wave-lengths varied from 0.08 to 0.70 Angstrom units. It is obvious that the course of the curve is not changed at all when the wave-length is varied within these very wide limits.

Braun and Holthusen (12) have recently made similar experiments on Ascaris eggs and have come to the same conclusion. An important point which they emphasize is that the course of the mortality curve changes somewhat with the length of the dose; that is, there is a time factor which must be considered, the effect of which had previously been investigated by Liechti (62). A dose which kills 50 per cent of the individuals may be given in a short time or over a long period in fractions. In the latter case the development of the eggs is held in check by keeping them under anaerobic conditions. The curve is now flatter than in the first method, and resembles the theoretical curve demanded when large quanta are used. This factor may explain some of the results obtained by other investigators.

This part of the theory, then, is not supported by the results of these extensive experiments. A further difficulty in its acceptance lies in the sudden changes in susceptibility during mitosis. To explain this situation one might postulate that the sensitive spot grows larger during cell division and thus is more likely to be hit; or else that its nature has changed so that it may be destroyed by a variable number of hits, depending on the stage in mitosis during which irradiation is given. Either possibility introduces a factor which the theory is framed to avoid, namely, variation in the biological material. In its present form it appears untenable, but it is a valuable contribution to radiology, since it calls attention to certain physical conceptions which biologists must take into consideration when attempting to explain the effects of radiations.

VIII

QUANTITATIVE EFFECTS OF DIFFERENT WAVE-LENGTHS

For many years the question of the relative effectiveness of long and short rays has been debated by radiotherapists, who must use both kinds in their work. In skin therapy the long, non-penetrating rays are employed because they give up their energy at the surface; in deep therapy, such wave-lengths are chosen as will penetrate to the desired place. If beams of widely different qualities have the same intensity,—that is, if they produce the same amount of ionization in air,—will their total biological effect be the same or will one be more effective than the other. The question is of great practical importance, for if there is a difference, then the problem of dosage becomes very complicated.

The general opinion has been that long rays are more effective in producing an erythema (119), but recent work shows that this is not strictly true (27). If small areas of skin are exposed to equal doses of long and short rays the amount of reddening is the same in all. This test is not ideal for solving the problem because of the high degree of variability in human patients, and because the depth of the absorbing tissue is necessarily different in the two cases. The long rays

are absorbed in a few millimeters of tissue; the short, in several centimeters. A better method is to use small objects, such as cells, or eggs of Drosophila or Ascaris in which the question of penetration does not arise.

Dognon (29), who used Ascaris eggs, concluded that moderately soft rays are least effective, while rays both shorter and longer than these are more potent. Some doubt is thrown on these results by Dauvillier (25), who shows that Dognon's computations of the intensity of the beams were wrong. Zuppinger (125), who reviews the subject at length, comes to somewhat the same conclusion as Dognon, but finds that the increase in effectiveness of the very long rays is slight. On the other hand Bolaffio (9) arrives at the opposite conclusion, for he reports that long waves are more effective than the short.

Some of these discordant results are almost certainly due to inadequate methods of measuring intensities at widely different wave-lengths. The ionization chambers which were used were not accurate throughout the entire range, registering too low at some points and too high at others. When, however, measurements are made with a large, open, air ionization chamber of the type now recognized as free from these errors, the biological effect of beams of different qualities is found to be the same.

This was first clearly demonstrated by Wood (121, 122), who used as a test object finely minced tumor tissue which after irradiation was inoculated into healthy animals. The criterion of effect was the percentage of "takes." If no tumors grew after inoculation the cells had received a lethal dose. In all of the many tests with different tumor strains the conditions of exposure were carefully regulated so as to ensure perfect constancy of output from the tube. For example, the current was continuous, not fluctuating as in the case of machines having mechanical rectification. The two beams used for experiment were nearly homogeneous in wave-length (0.68 and 0.22 A. U.). The results show that when the tumor cells of any particular strain are exposed to these qualities of radiation, the doses varying from subminimal to lethal, the proportion of takes which result lie along a single curve. In other words, the biological effect is correlated with the degree of ionization as measured in air. And since this is practically the same as in tissue, the conclusion must be drawn that the amount of ionization in tissues determines the amount of effect, regardless of wave-length.

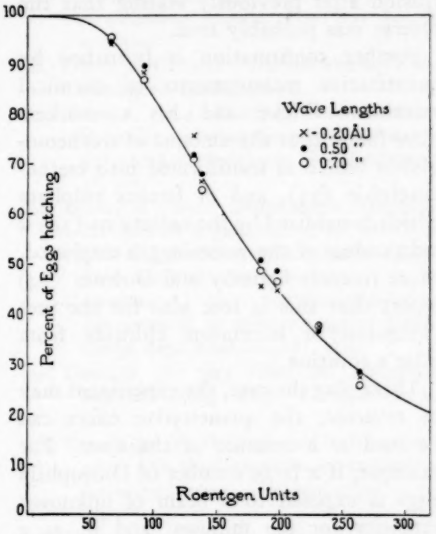

FIG. 5. AN EXPERIMENT SHOWING THAT X-RAYS OF DIFFERENT WAVE LENGTH ARE EQUALLY EFFECTIVE BIOLOGICALLY

Subsequently I repeated these experiments (75), using Drosophila eggs in place of tumor cells, and employing a third wave-length intermediate between

the two used by Wood. While the sensitiveness of these eggs is far greater than that of any of the various kinds of tumor cells,—to reduce the number of takes to 50 per cent requires from six to eleven times as many Roentgen units as to kill half of a sample of Drosophila eggs,—they reacted in the same way. Equal doses, measured by the large ionization chamber, kill equal proportions of eggs. Holthusen (46) comes to the same conclusion after previously stating that the reverse was probably true.

Further confirmation is furnished by quantitative measurements of chemical reactions. Fricke and his co-workers have found that the amount of oxyhemoglobin which is transformed into methemoglobin (33), and of ferrous sulphate which is oxidized by the radiations (34) is independent of the wave-length employed. More recently Quimby and Downes (84) report that this is true also for the precipitation of mercurous chloride from Eder's solution.

This being the case, the experiment may be reversed; the quantitative effect can be used as a measure of the dose. For example, if a large number of Drosophila eggs is exposed to a beam of unknown intensity for ten minutes, and if, as a result, half of the individuals fail to hatch, then 180 Roentgen units must have been delivered at the rate of 18 r/min. (76). Many tests made during the past few years have shown that a carefully measured dose of this size always gives this result, the variation being less than 5 per cent. In the same way Quimby and Downes (84) use their chemical method and find that the results when compared with ionization tests are correct within a few per cent.

Reasonably precise measurement of dosage is essential in any experiments regardless of whether they are quantitative in nature or otherwise. Without it, one can never be certain that the dose he gives is really what he supposes it to be; and for another to repeat the work accurately is almost impossible. The older methods of defining dosage by stating the voltage, filtration, and amperage are of very restricted value because different machines differ so widely in their output even when these factors are supposedly the same. This is because the current in some is interrupted, in others it is nearly continuous; because the output of tubes varies with their age and the thickness of the glass; because the meters are by no means accurate; and because the intensity of the beam varies within wide limits, depending on the way in which the control board resistance is adjusted (79).

Fortunately it is possible now to measure intensities with ease and with fair accuracy (13), and to determine the number of Roentgen units delivered during exposure. When this information is given, together with the voltage and filtration, anyone may obtain the same dose on another machine. The mention of the latter data is important, not because the effects of the primary beam vary with the different qualities but because the penetration varies and so also does the amount of back-scattered radiation.

The accurate measure of dosage in Roentgen units reduces the number of variable factors in the experiment. One which cannot now be excluded is that of biological variation; but if this is measured properly and taken into account, sound conclusions may be drawn regarding the effect of radiations on living matter.

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QUANTITATIVE RELATIONS IN BIOLOGICAL PROCESSES AND THE RADIATION HYPOTHESIS OF CHEMICAL ACTIVATION

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I

THE PROBLEM

CORRELATION between photochemical reactions and Planck's quantum theory of radiant energy has been the subject of many investigations since that early work of Stark in 1909, of Einstein in 1912, and the experiments of E. Warburg in 1912 and M. Bodenstein in 1913 (1). It was a natural next step to investigate the phenomena of photochemical reactions occurring among living things (2); and when once the idea became clear, that wherever reaction is caused by radiant energy of any kind there probably will be reaction per quantum, determined by the frequency of the absorbed radiation, then a widespread search got under way for the correlations between atomic and molecular exchanges and the quanta of non-luminous, or thermal, radiations. Trautz (1906–1918); Haber, 1911; Baly, 1913; Perrin, 1919; W. C. M. Lewis, 1919; G. N. Lewis and D. F. Smith, 1925; Tolman, 1925, and others made important contributions to the facts and theory in this very interesting field of chemistry (3).

The difficulties of applying the quantum theorem to chemical reactions that proceed in condensed systems have been considerable; the difficulties in its application to heterogeneous systems, to colloidal suspensions in liquids, must be accordingly all the greater. There would seem to be no way to measure either emitted, incident or absorbed radiation in systems where the source of radiation, as well as the absorption, is within the system itself. In the study of photochemical processes in living matter the source of light in most cases can be controlled, and the quantity absorbed in many cases can be measured; and while no demonstration has been made of the direct validity of the equivalence law, yet the relations between molecular and quantal exchanges that have been shown in these investigations are of the greatest interest, and suggest further that similar studies of darkfield or non-luminous reactions in living matter may yield results of no less interest. The measure of molecular exchanges in such systems has offered comparatively little difficulty. As for the measure of quanta the difficulty is obvious and every method will meet serious objection (4). But as a preliminary working hypothesis we may assume that during a physiological action all or an aliquot part of the radiational energy exchanges have their counterpart in the form of external work, or in heat, or both; the work and heat may be observed by appropriate methods.

Finally either an arbitrary value may be assigned to the unknown frequency characteristic, or the frequency may be calculated from the reverse statement of the law of equivalence. In the former case the frequency is assumed from Wien's law of displacement and the quanta are calcu-

lated; in the latter case the ratio of quanta to number of activated molecules is assumed to be unity, the calculated frequency from which is compared with that demanded by theory.

As to the possibility of the law of quanta holding among physiological processes one need only recall the Weber-Fechner law of stimulation. This "law" was based upon the observation that increasing stimuli have increasing effects only when the energy of the increased stimulus has reached a certain new level, in other words that stimuli are effective in jumps rather than in continuous gradations. The all-or-none law among physiological processes in last analysis likewise may turn out to have its final explanation in the theory of quanta (Pratt and Eisenberger, 2). Indeed Zwaardemaker (2, 1927, p. 252) urges the reinvestigation of this class of phenomena from the viewpoint of the quantum theorem and the radiational hypothesis as being well worthwhile.

In the explanation of the sensitizing action of some dyes, as developed by von Tappeiner (2), it is assumed that ultra violet frequencies are somehow emitted and act on the absorbing protoplasm. Gurwitch (2) explains his observations of increased mitosis and cell division in one growing root-tip, when near another growing tip, by assuming that radiant energy, sent out from the one tip, is absorbed by the other. Finally the radioactive phenomena as observed by Zwaardemaker (2) in his long series of researches all suggest that living matter is continually under the influence of radiations of many sorts that from time to time take on effective or critical frequencies.

After this essay was practically completed a title indicating a similar study came to my attention, namely, the dissertation of L. B. Becking (2) on "Radiation and Vital Phenomena," a copy of which finally came into my hands. In this work the author has examined some physiological reactions, especially those that are influenced by both light and heat, and finds that the calculated wave-length often corresponds to the incident wave-length optimal for the process, or to the wave-length of maximum absorption by the proteins involved in the tissue observed. The treatise rather fully describes the equations underlying the applications of the radiational hypothesis to chemical reactions, following the reasoning of Ornstein, Perrin and Tolman. When the rates of reaction at different temperatures are the data used in calculating the energy transfer, the equation of Perrin, namely, $\lambda = \rho \cdot \frac{6.2}{T_1(T_1 + 10) \log_{10} Q_{10}}$ is employed, where 6.2 is the product of a number of radiation constants and ρ is Perrin's constant, which is made equal to 1 for cases where the usual temperature coefficients hold, and < 1 for cases where the higher coefficients obtain ($\rho = 0.27$ in Becking's cases!) and then called a modification constant. Q_{10} is the usual temperature coefficient of rate of reaction for temperatures 10° apart.

The above equation has its fundamental derivation in (a) Planck's luminosity equations and (b) in the van't Hoff-Arrhenius equation for influence of temperature on chemical reaction rates. For it has been shown theoretically (Trautz, Marcelin, Rice, Lewis, Perrin, Tolman) that for cases where light is absorbed (a) may be written finally

$$\ln q = \rho \frac{h\nu}{k} \left(\frac{1}{T_1} - \frac{1}{T_2} \right) \qquad (1)$$

and that (b) may be written,

$$\ln q = A \left(\frac{1}{T_1} - \frac{1}{T_2} \right) \qquad (2)$$

for dark body reactions. Now since $\rho h\nu/k$ in the one, and A in the other, are expressions of energy differences, in the first case for known light absorption, in the second case for assumed black body (thermal) radiations, factor, A, in the case of chemical reactions may be replaced by $\rho h\nu/k$; equation (2) then enables one to calculate the frequency or wave-length of the dark body reaction directly, since the energy of activation, q, may be calculated from the rates of the reaction. Among those vital processes whose light-responses are influenced by temperature, Becking shows that in many cases the calculated wave-length is in close agreement with the wave-length observed to be absorbed.

In the present paper attention will be directed especially toward those physiological processes in which no visible light is known to play a rôle directly, but whose rates of reaction are markedly influenced by temperature. In these cases it will be assumed that the energy increment is due to an increase of the mean infra-red frequency, and, therefore, that the laws for dark-body radiation hold. The phenomena investigated will be those that belong to the category of physiological stimuli as well as responses, although the latter class will receive more attention. Since all these processes go on in condensed, and often heterogeneous, sometimes suspensoid systems, doubt will be raised as to whether the laws of (infra-red) radiation actually hold, or if they appear to hold, whether any meaning could be attached to the result. For answer the reader is referred to the discussions of the physical chemists and especially to those of the champions of the radiation hypothesis of chemical reaction (3, 4).

If the energy increment, q, of a (gram-molecular) chemical reaction is due to a critical increment in radiational frequency then q should be equal to $Nh\nu$ as Einstein postulated for pure photochemical reactions, and if it is not, we may show at least what the disparity is in the two values for the physiological reactions considered. Rather than calculate the frequency according to the method of Tolman and Perrin it seems more desirable to assume the frequency to be that indicated by Wien's displacement law, and the physiological reaction to be of a dark-body radiational nature. In this case then the treatment will follow more nearly the original suggestions of Trautz, Marcelin and Haber.

II

QUANTUM RELATIONS APPLIED TO LIVING PROCESSES

1. *Respiration metabolism and photosynthesis in plants*

We take up the cases where the gram molecular heat of activation, q, of the van't Hoff-Arrhenius equation is compared with the gm. mol. quanta, $Nh\nu$. Here, as stated above, q is the energy value of the difference in maximal frequencies leading to the reaction, or the $E - E'$ difference of Haber (3). The median critical frequency concerned in the reaction is arbitrarily assumed to correspond to the median temperature, and as indicated by Wien's displacement law, $\lambda\mu \cdot T = 2882$. The inquiry then turns on the relation between $q/Nh\nu$ in all those cases where rates of reaction or response are known at different temperatures between range limits compatible with normal living matter.

In practice the equation used is in the form,

$$q = \left(\log_{10} \frac{k_2}{k_1}\right) \frac{R}{0.4343} \cdot \frac{T_1 T_2}{T_2 - T_1}$$

or, in cases where the temperature coefficient, Q_{10}, is already known,

$$q = (\log Q_{10}) \cdot 4.57 \cdot \frac{T_1(T_1 + 10)}{10},$$

of which a close approximation is to be had, when T is put median to T_1 and $T_1 + 10$, by the expression $q = 0.46\ T^2 \log Q_{10}$.

Data on plant metabolism will come first in order, since photochemical reactions in plants have been studied already from the quantum point of view, and since a fairly large body of measurements of dark-field reactions of the same proc-

esses also have been made which we may use for comparison.

Among these latter is the work of Kuijper (5), who observed the CO_2 given off by seedlings of *Pisum sativum*. At 10° there were 11.275 mgm.; at 20°C, 30.4 mgm were given off. Applying our equation,

$$q = \log \frac{30.4}{11.275} \cdot 0.457 \cdot 283 \cdot 293 =$$

16,280 calories

From Wien's law $h\nu$ at T_m of the observations will be $19.55 \cdot 10^{-14}$ ergs. Putting the Avogadro number equal to $6.06 \cdot 10^{23}$ and 1 cal. $= 4.19 \cdot 10^7$ ergs, $q/Nh\nu =$ 5.67 quanta per molecule of CO_2 expired by the seedlings.

Yabusoe (5) showed that the O_2 used up by *Chlorella* is independent of visible radiation, but on the other hand is a logarithmic function of the temperature between certain limits. The breathing of plants, thus, as in animals may be viewed as a function rather of thermal radiation than radiations of the visible spectrum. The oxygen intake for *Chlorella* was found to be 38 cmm. at 10°, 71 cmm. at 20° and 147 cmm. at 30°C. From these data $q =$ 11,500 calories and $q/Nh\nu = 3.99$ quanta per molecule of oxygen used up by the plant at the median temperature.

The influence of temperature upon the process of photosynthesis in plants has also been studied. In this case the radiational frequencies are more complicated, and the story of the experimental and theoretical attack on the problem is of the greatest interest. Let us start with the naïvest of considerations, the quanta yield of the thermal radiations as given by the data observed at different temperatures. Matthaei (5), who was one of the first to observe this, found that the green leaf of *Prunus laurocerasus* in the light and at 37° absorbed 23.8 mgm. CO_2 and at 0° absorbed only 1.75 mgm. Putting these figures through the mill of the Arrhenius equation indicates a value of $q =$ 11,940 calories per gm.-mol., and when $h\nu$ is taken at 20°C a value of $q/Nh\nu = 4.0$ quanta per molecule of CO_2 assimilated by the green leaf. Similar treatment of the data of Osterhout and Haas (5), who studied a species of the marine green alga, *Ulva*, indicates a yield of 3.6 thermal quanta per molecule of CO_2 reduced during photochemical processes going on in *Ulva*.

The results of O. Warburg (5) in his reinvestigation of the Blackman reaction are of still greater interest. It will be remembered that Blackman found that the temperature coefficient for CO_2 absorption by green plants is in part a function of the intensity of the incident light, temperature having little or no influence when the intensity is low enough, but having a very pronounced influence for the higher intensities. In the following table the data of Warburg are reproduced, to which I add my calculations of the quanta yield as revealed by the thermodynamic equation for each small range of temperature. It will be noted that not only do the dark-field quanta-yields vary as do the Q_{10} values but also that they are both higher in the experiments where the light intensity is higher and lower when the intensity is lower. The remarkable thing is that the thermal quanta yields (and Q_{10} values) are for the most part whole numbers, within the probable experimental error, for the higher intensities of light.

Table 1 again gives the evidence of Warburg that at the lowest intensities of light the heat surrounding the plants adds nothing to the energy of the reaction.

It is to be regretted that the range of temperature for each of the four intensities tried was not coextensive; the conclusion to be drawn would have had greater certainty. For example Q_{10} for the range 25° – 32° is not given for any intensity excepting the lowest (I = 1) and it is obvious that Q_{10} for I = 1.8 probably would be equal to 1.0 for temperatures 25° – 32°; but since the value of Q_{10} tends always to rise with the fall of T, then will that not also be the case for I = 1? In other words one can only be certain from the data of Warburg that it is only for the highest temperature and probably for the lowest effective light intensity that the surrounding heat adds nothing to the energy of the photosynthesis. It is of no little interest that the thermal quanta, or $q/Nh\nu$ value, for the median temperature range and the higher light intensities is nearly equal to the light quanta found by Warburg and Neglein (2) in their direct and simultaneous measurement of light and CO_2 absorbed by *Chlorella*, namely 4 and 5 quanta per molecule of CO_2 reduced, respectively, by the two different portions of the spectrum they tried. It is also a striking fact that this finding for median thermal quanta for the photosynthetic process is nearly of the same magnitude as that found for the reverse process, the expiration of CO_2 by green leaves (Kuijper, *v. supra*).

TABLE 1

The heat of activation in terms of quanta for photosynthesis in Chlorella. After the data of O. Warburg

	TEMPERATURE RANGE, DEG. C.						
	5–10	16–25	5.4–10	10–20	20–30	15–25	25–32
Relative intensity of light	16	16	45	45	45	1.8	1.0
Q_{10}	4.8	2.0	4.3	2.1	1.6	1.06	1.00
Heat in cal., (q)	24,500	11,570	22,700	12,400	8.260	1,110	0
$q/Nh\nu$	8.8	4.0	8.2	4.36	2.88	0.384	0

2. *Oxidation and reduction phenomena of haemoglobin and allied substances under dark-field and visible illumination*

The haemoglobin (Hb) of animals has been associated with chlorophyll of plants in the minds of biologists for a long time; it is appropriate that we consider its functional chemistry at this point. The material on haemoglobin at hand enables us to get at the thermal quanta in a somewhat different way. From the work of Hüffner and Gausser (5) the least molecular weight assignable to Hb is 16,669. From the work of R. du Bois-Reymond (5) the heat of the reaction when Hb combines with O_2 is 1.36 calorie per gm. Hb. The gm.-molecular heat accordingly may be put at 22,670 cal. whence, with $h\nu$ at 20°C, $q/Nh\nu$ = 7.85 quanta per molecule of oxygen in the reaction. If the observation of Torup (5) namely, 0.678 cal. per gm. Hb is the correct figure for the heat of reaction then the quanta yield is 3.92 per molecule of Hb. It will be noticed that the figure of R. du Bois-Reymond is just twice that of Torup. The heat liberated by the absorption of O_2 by whole blood was observed by Camis (5), who on the basis of his data put the heat per gm.-mol. of O_2 observed at 10,220 cal. At 20° on this basis $q/Nh\nu$ = 3.54.

The influence of temperature upon the absorption of O_2 by the red cells of geese was observed by Meyerhof (5). At 38.1°, 1.29 mgm. and at 18.6°, 0.319 mgm. were

absorbed; whence q = 13,100 and the quanta yield is 4.5 per molecule. Again the observations of Barcroft and King (5) on haemoglobin solutions when the pressure of O_2 is kept constant at 10 mm. Hg. show that 93 per cent saturation obtains at 14° and 14 per cent saturation at 38°C; whence q = 10,370 and the quanta yield is 3.6 per mol. at temperature 20°. Since the quanta yield as gotten from the data of Torup, Camis, Meyerhof, Barcroft and King all indicate lower values than that gotten from du Bois-Reymond's data and since the difference is roughly as 1:2:3, it would appear that we are dealing with polymeric forms of Hb.

The effect of sun light, as observed by Haldane and Smith (5), upon the reaction equilibrium, $\frac{[O_2]}{[CO]} \cdot \frac{[HbCO]}{[HbO_2]}$ arouses one's interest to an even greater extent; for the foregoing phenomena thus far have involved only the grosser thermal radiations. Hartridge and Hill (5) reported observations showing that the reduction of HbO_2 by CO was diminished not by the visible rays of the sun's light but by that portion of it represented by wave lengths lying between 850 and 1075 mμ, all of which are within the infra-red. The energies of these wave-lengths, when expressed in gram-molecular quantities calculated from $Nh\nu$, lie between 33,560 and 26,580 calories, the mean of the extreme values being 30,140 calories. Now it is a striking fact that the heat of activation of the reaction $Hb + O_2 \rightarrow HbO_2$, as calculated by Barcroft and Hill (5) from their observations on rate of the reaction at 18° and 38°C, was found to be 28,000 calories, a figure corresponding to the less energetic half of the wave-lengths absorbed by haemoglobin as observed by Hartridge and Hill. If we conceive of the CO molecules in the above system as furnishing enough energy to overcome the combination HbO_2, it probably must be something more than 28,000 calories; and in turn, if the reducing effect of the CO molecules is to be counteracted, it would be reasonable to suppose that an energy source somewhat greater than 28,000 calories would have to be available. It appears that the infra-red radiations, whose mean energy complement is 30,140 calories, are able to diminish the reducing power of CO in the $Hb + O_2 \rightarrow HbO_2$ reaction because the energy they bring to bear is just more than enough to counteract the energy of the CO molecules. One may express this triangle of mutually antagonistic forces thus:

$$Hb + O_2 + 28{,}000 \text{ cal.} \rightarrow HbO_2$$
$$HbO_2 + CO - 29{,}000 \text{ cal.} \rightarrow HbCO + O_2$$
$$HbCO + O_2 + 30{,}000 \text{ cal.} \rightarrow HbO_2 + CO$$

The closeness in value of the counteracting energies may account for the fact that the reactions under ordinary conditions are never complete and that the radiations observed to be absorbed diminish the reducing power of CO on the HbO_2 compound only 1/20 to 1/36 of its reducing power in the presence of the longer wave-lengths. It would appear that the law of equivalence may be valid in this reaction, and only awaits experimental evidence to prove it.

This section should not be ended before mentioning certain data obtained by Gaffron (5) on chlorophyll and haematoporphyrin. When chlorophyll is dissolved in acetone and treated with light it is found that O_2 is absorbed by the chlorophyll in such quantities that the relation between O_2 and light absorbed is not only a constant but a constant approaching unity, the figures being 0.97, 1.01, 0.97, and 0.99 for red, yellow, green and blue light. Gaffron, who did this work in O. Warburg's laboratory, also showed that haematoporphyrin and other

fluorescent substances obey the law of equivalence. The quanta yield for haematoporphyrin and allylthiourea is of the order of 0.99. When acceptor is added the yield is made to deviate from 0.1 to 0.86.

Putting these remarkable facts together with the performances of chlorophyll and haemoglobin in their more normally vital activities it would seem that thermal radiations must play some important rôle in the latter that should be demonstrable by further experiments designed expressly for the purpose.

3. *Quantum relations among the obscurer physiological processes, the limits of their validity*

Having examined a few of the more obvious biochemical reactions let us now turn our attention to some of the obscurer physiological processes. Of these there are some that (it would seem *a priori*), when once revealed, will be found comparatively simple of explanation. To this group there are (1) the inner stimulus that gives rise to automatic rhythms of various sorts, (2) the true latent periods intervening between the moments of stimulation and response, and (3) the conduction of the excitatory process in muscle and nerve or indeed in protoplasm in general. It was after a consideration such as this that many of my studies on temperature coefficients have been directed toward these processes. It has been objected that temperature coefficients of such phenomena are meaningless because of the complexity of the phenomena, and that the many physical factors involved set limits to rates of reaction that in turn obscure the real rates of chemical action; finally, that the coefficients in any case hold for only a limited range. The answer to all these criticisms may some day be given in full. Here I wish only to answer briefly.

First, there probably are no physiologists who have not thought of these limits; second, the objections offered hold even for "pure" homogeneous chemical systems, temperature coefficients always hold approximately for only limited ranges of temperature in the inorganic world. The Arrhenius equation, $\frac{k_2}{k_1} = e^{\frac{T_2 - T_1}{T_1 T_2}}$ allows for a variable temperature coefficient, and thus Q_{10} decreases between the physiological limits as the temperature increases. Finally it hardly needs to be pointed out that the temperature coefficients for expansion, and of electrical conduction for metals change as soon as solids melt or liquids congeal; the gas laws themselves have limits. It would not be strange then if temperature coefficients change when lipoids congeal at lower or liquify at the higher temperatures; when the solubilities of gases (oxygen and carbon dioxide) and viscosity of protoplasm increase inversely, diffusion rate directly, with temperature. The many studies that have appeared, in which these and others of the various physical factors involved have been investigated as to their specific rôles, are highly commendable but none of them have succeeded in changing the general proposition that in many cases, within certain ranges of temperature, the temperature coefficient is an index as to whether or not a physiological process is fundamentally of a physical or a chemical nature. And with temperature coefficient we include the Arrhenius formula; for the coefficient as well as the formula are both based upon the van't Hoff reaction isochore, the most fundamental of all formulae in chemical thermodynamics. It was with this understanding that both the heat of

activation (either as a half value, as in the term A, or as its whole value, as in the term q, or μ, in the Arrhenius formula) and temperature coefficients have been calculated in most of my papers from the very first published on the subject.

With this understanding then of the limitations imposed let us proceed to a consideration of the quanta relations of some of the simpler physiological processes of obscurer character.

4. Quantum relations among the rhythmical processes

It was my privilege in the years 1904–1908 to be among the first to demonstrate that certain of the unexplained physiological processes, in their rates of reaction as influenced by temperature, obey the rule of van't Hoff-Arrhenius, within certain limits and behave, therefore, like purely chemical systems. In a summary of some fifty such cases (6, 1908) it was pointed out that the heat constants in the Arrhenius equation tend to be of the same ranges of magnitude as had been found for many chemical reactions, that there is a tendency for the values to be the same for physiological processes of like character, and finally that there is a suggestion that the heat values (expressed there as $\mu/1000$) fall into multiples of four. (See the last column in the tables on pp. 330–333 of my 1908 paper on "A Comparative Study of Temperature Coefficients," cited above.) At the time I had no explanation to offer for this tendency and so did not discuss the point. In the light of the quantum theory, however, there seems to be some possible explanation. One's curiosity concerning the cases brought together in that initial list will be satisfied on this point perhaps when I say that of 17 of the more reliable observations on the spontaneous rhythms of muscular organs the quanta yields vary from 4.0 to 6.9 with a mean value of 5.5, and that only eight out of the 17 yield figures for quanta that are nearly whole numbers. The eight cases yield quanta of 6.08, 4.05, 6.91, 5.08, 5.00, 4.13, 6.02 and 6.12. It is thus clear thus far that one can attach no significance to their whole-number character.

Of the later studies on rhythmic processes there are three different groups that may be recalled with profit. First there is the series of experiments on the isolated mammalian heart that I carried through with the aid of two of my students, Messrs Elmendorf and Fallas (6, 1913). In one case a dog's heart beat for hours at very widely different temperatures; the plotted rates fall about a logarithmic curve the extreme points of which give a rate of 35.2 at 23.5° and 116 at 40.4°C. The heat of activation, q, in this case equals 13,270 and the ratio $q/Nh\nu$ at 32° yields 4.43 quanta. In the same series a cat's heart beat with rate of 18.5 at 20° and 122 at 40°C, whence q = 17,400 and $q/Nh\nu$ (with thermal frequency taken for 30°C) gives 5.85 quanta. A second study is one on the flashing interval of fire-flies (6, 1920). The observations were made on successive evenings during one summer and thus at various temperatures. At 28.55° the rate of flash was found to be 15.2 times per minute; at 19.4°, 8.1 times per minute. Whence one calculates 4.15 quanta at 24°C per molecule of the stuff that sets off the nervous reflex producing the flash in the fire-fly.

Locomotion in animals is a sort of rhythmical activity and after once started is maintained doubtless with comparatively simple mechanism so long as no complicating factors intervene. For a discussion of this point see my paper of 1904 (6). A number of researches have been published on the influence of temperature on the rate of locomotion. For

our third type of rhythmicity however I take the results of only one of the more recent studies, that of Shapley (6). This observer finds evidence of an abrupt change from one value to another of the temperature coefficient for 10-degrees interval and argues that if two reactions (among the many involved) limit and control the resultant temperature coefficients, then the μ ($\equiv q$) values may be indices of this. This author finds for the species of ant, *Liometopum*, $Q_{10} = 3.3$ at the median temperature, $T_m = 288°$ abs., and $\mu = 19{,}800$; with $Q_{10} = 1.9$, $T_m = 302°$ abs., $\mu = 11{,}700$. At these two values of T_m, $Nh\nu =$ 2833 and 2965 calories respectively whence the quanta yield at the two energy levels become 19800/2833 and 11700/2965, or 6.99 and 3.94 respectively, both figures being whole numbers within 1.5 per cent as extreme variations.

As a final example of rhymicity I take one from the inorganic world, the phenomenon of rhythmicity in passive iron as observed by R. S. Lillie (6). After once setting up a wave of activation on a suitable ring of passive iron wire the activity is maintained by the first wave automatically giving rise to another indefinitely. The rate of rhythm at 10° is about 15, at 30° about 125 per minute, representing a q-value of 18,190 calories and a quantum yield at the median temperature of nearly 6.3 per molecule, or ion, of the substance responsible for the rhythmical oxidation-reduction phenomenon.

5. *Quantum relations in the processes of conduction of the excitatory state*

Let us now pass on to a consideration of the phenomenon of conduction. As data I shall take the results of my study of the influence of temperature upon the velocity of impulse in frogs' motor nerves (7). In the accompanying figure the curve connects the statistical means of the observations at temperatures about five degrees apart. The interrupted line, continuing the curve a distance for the higher range of temperature, represents the velocity of conduction in mammalian motor nerve as observed by Professors Erlanger and Gasser and their associates (7), and is added only as giving evidence that the nature of motor nerve in both classes of

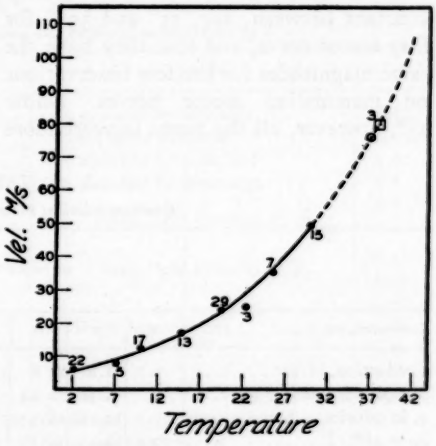

FIG. 1. MEAN VELOCITIES OF CONDUCTION AT VARIOUS CORRESPONDING MEAN TEMPERATURES

Those for frog's sciatic nerves are shown by the symbols, • • • •, and represent 111 observations on nerves from 12 different fall frogs (Snyder, 1908). The symbol ⊙ is the observation of Felix (1923) on the motor-sensory nerve-trunk in the leg of man. The symbol ⊡ is the mean of three determinations by Erlanger and Gasser (1924) on the dog's tibial nerve. The numerals attached to the symbols indicate in each case the frequency of the observation.

vertebrates is probably very much the same.

In the following table I have assembled the various values that may be calculated from these data, taking points exactly five degrees apart on the smoothed curve. The symbols in the first column stand for velocity of conduction in meters per second, M/Sec.; temperature coefficients for intervals of ten degrees, Q_{10}; heat of

activation in calories as calculated from the Arrhenius equation, q; the assumed effective radiation wave-length in thousandths of a mm. for each temperature as determined by Wien's displacement law, $\lambda\mu = 2882/T$; and finally the quanta yield per molecule of the hypothetical substance primarily involved in the probable physico-chemical reaction, $q/Nh\nu$.

From table 2 it is seen that these mean values of Q_{10}, q and quanta are all pretty constant between, say, 15° and 35°C for frog motor nerve, and that they have the same magnitudes for the few observations on mammalian motor nerves. Below 15°, however, all the terms increase more or less abruptly so that between 2° and 12° they have values markedly greater than any variations in their values between 12° and 42°; the increase being in round numbers 10 per cent for Q_{10}, 16 per cent for q, 25 per cent for the quanta yield. This more or less abrupt change in the q value is what Crozier (7) has referred to as a change in "temperature characteristic," or in "critical increment," a term he uses "to provide a name for the E or μ in the van't Hoff-Arrhenius equation, which should be free from the connotation of any particular view as to the mechanism of activation." But, as the reader sees, the increase in quanta yield appears to be the more significant, the average of the mean values for the temperature range above 12° being 4.16, whereas the value for the range from 2° to 12° is 5.18, a gain of a whole quantum.

But there may be objection to assuming the wave-length to be that corresponding to the prevailing temperature; it may be assumed rather that the law of equivalence holds, in which case $q = Nh\nu$, and (since q, N and h are known) that the radiation frequency should rather be calculated from this latter equation. In this case the effective wave-length turns out to be 1/5 and 1/4 less than those assumed in the table above, that is, $\lambda\mu =$ 2 and somewhat > 2. These are still in the infra-red but correspond to temperatures much higher than the observed. Now such radiation frequencies are not impossible any more than the still higher ones that are absorbed in the "cold" photochemical reactions. Nevertheless since the frequencies in the latter correspond beyond doubt to those portions of the spectrum that are known to be absorbed, whereas the only known radiations concerned in nerve processes are those corresponding to the observed temperatures, we must believe, until contrary proof is adduced, that the longer wave-lengths given in the table above are

TABLE 2

Quantum relations in rate of motor nerve conduction

	OF FROGS' SCIATIC NERVES							OF DOG'S SKELETAL MOTOR NERVES		MEAN BETWEEN 12° AND	MEAN BETWEEN 12° AND
Temperature, deg. C.	2	7	12	17	22	27	32	37	42	42°	32°
Conduction, M/Sec.	5.7	8.8	13.6	19.7	27.8	40	56	76	106		
Temperature coef., Q_{10}		2.38	2.24	2.02	2.07	2.07	1.90	1.89		1.99	2.05
q, in calories		14,260	12,970	12,200	12,250	12,480	11,880	12,430		12,248	12,310
$\lambda\mu = 2882/T$	10.4	10.25	10.10	9.93	9.77	9.60	9.45	9.30	9.16		
$q/NH\nu$ = quanta		5.18	4.63	4.28	4.24	4.24	3.97	4.08		4.16	4.25

more probably the ones absorbed. This latter conclusion is supported further when we recall that even in photochemical reaction of the green plant as observed by Warburg and Negelein (see above), the quanta yield did not turn out to follow the law of equivalence, but had the values 5 and 4, values nearly the same as we here find to be true for nerve conduction from its thermo-chemical reaction.

From the observations of R. S. Lillie (7) on the influence of temperature on rate of conduction of the activation wave in "passive" iron wire the quantum yield appears to be of a similar order.

6. *Summary of the findings of Chapter II*

In table 3 I have summarized the quantum yield thus far revealed by this analysis of various physiological processes.

TABLE 3

Summary of mean ratios of thermal quanta and number of molecules acting

OBSERVER	CTIVITY	$q/Nh\nu$
Kuijper, 1910	CO_2 given off by seedlings	5.67
Yabusoe, 1924	O_2 used up by chlorella	3.99
Matthaei, 1904	CO_2 absorbed by green leaf	4.0
Osterhout and Haas, 1919	CO_2 absorbed by green alga	3.6
Warburg, Q., 1919	ditto, light intensity = 16	8.8 4.0
	ditto, light intensity = 45	8.2 4.34 2.88
R. du Bois Reymond, 1914	Oxidation haemoglobin	7.85
Torup, 1906	ditto	3.92
Barcroft and King, 1909	ditto	3.6
Barcroft and Hill, 1910	ditto	9.96
Camis, 1907	Oxidation of defibrinated blood	3.54
Meyerhof, 1912	Oxidation erythrocytes	4.5
Snyder, *et al.* 1908	Muscular rhythmical contractions, 17 experiments, extremes	4.0 6.9
Snyder, *et al.*, 1913	Rate of heart beat, dog's	4.43
	cat's	5.85
Snyder, *et al.*, 1919	Flashing interval, fire-flies	4.15
Shapley, 1924	Rate of locomotion in ants, 1925	6.99 3.94
Lillie, R. S., 1928	Rhymicity in passive iron	6.3
Snyder, 1908	Rate of conductivity in motor nerves	4.16
		5.18
Rosenberg and Sugimoto, 1925	ditto	4.27

In passing it may be pointed out that the researches of Tanaki (7) and of Rosenberg and Sugimoto (7) working in Professor Cremer's laboratory have disposed of the doubt raised by Broemser (7) concerning the reality of temperature affecting conduction rate in nerve. The results of Rosenberg and Sugimoto indicate a similar quantum yield, namely 4.27.

It will be noted that the numerical values approach whole numbers within ± 20 per cent in 17 out of the 26 cases and that they all appear to lie within the limits of 3 to 10 quanta. If one refers to the summaries of quanta yields thus far determined for purely photo-chemical reactions, for example in Kistiakowaky's book (1), one finds that the results show much greater

deviation than obtains here among this group of physiological actions. Of course it should be remembered that all thermal chemical reactions, with temperature coefficients lying between 2 and 3, theoretically should give quanta yields of the order found in this table.

III

QUANTUM RELATIONS IN MUSCLE METABOLISM

In the foregoing chapter we have assumed that the q value of the thermodynamical equation expressing rate of chemical reaction is approximately a correct measure of the effective energy exchange in the reaction. In doing so we have relied upon observations of temperature and rates of reaction of the physiological processes as being all sufficient data for the determinations of the energy exchange, and, provisionally, therefore, of the radiation assumed to be absorbed or emitted. In the second section of Chapter II a few cases are given where both energy as well as amount of substance reacting are known in certain biochemical processes (absorption of O_2 by Hb). In the present chapter I wish to take up a few cases of the more complex processes in which both the energy and the material exchanges have been more or less completely measured, if not in one and the same experiment, at least in different experiments upon similar tissues and organs.

1. *The observed heat production and gaseous and carbohydrate metabolism of contracting cardiac muscle*

The heat produced in automatically beating heart has been a subject of frequent observation. The difficulty with this muscle as with smooth muscle has been to produce complete anaerobiosis. Experiments are now under way where (as more fully treated of below) the method applied to smooth muscle (8) is being applied also to the heart muscle. Until these redeterminations are complete we shall have to content ourselves with the earlier data and allow for the probable difference.

There seem to be few researches in the literature on the chemical changes going on in the beating turtle heart. On the other hand there is an embarrassing abundance of material in the literature on oxygen and carbohydrate metabolism of frog and mammalian hearts. When one surveys the results of these investigations and tries to reduce them to a common standard of comparison the task is almost hopeless. The problem is to find out from the data the quantity of oxygen used by unit mass of muscle per beat and per unit tension developed during that beat. Most of the data given are per unit weight of muscle per hour; often either the rate, or the exact temperature, is not given, nor is it always clear whether the volume given has been reduced to standard condition of pressure and temperature. The factor of tension, as I finally chose it, is the one in greatest doubt; in one or two cases it may be 200 per cent removed from the true value. When no data were given by the author from which tension could be calculated, I assumed 1 gm. muscle exerted 30 gm. tension. Bohnenkamp, Eismayer and Ernst (13) on the basis of their recent observations have concluded that tension has no influence on oxygen consumption of the heart, that organ being in this respect, as it is in others, all-or-none. However, this does not appear to be borne out by the work of Rohde and others and, until established by further investigation, cannot be accepted. In the table below the results of various observers have been reduced to a standard common to all,

that is, to the volume in cc. of oxygen used by 1 gm. muscle per beat and per 1 gm. maximum tension exerted during the beat. For the literature see note (13).

The oxygen used per gm. muscle per gram tension per beat by various kinds of hearts, in cc. $\times 10^{-6}$

Tortoise heart, Vernon (1910, CO_2 output observed; assuming R.Q. = 1)	3.7
Frog heart, Weizäcker (1912)	18.7
Lüscher (1920, 48.3; 1921, 38.7)	43.3
Bohnenkamp, *et alias* (1928)	33.0
Mammalian heart, Barcroft and Dixon (1907)	4.0
Rohde (1912)	17.0
Starling and Evans (1914)	14.6

With these it is interesting to compare the data for skeletal muscle in cc. $O_2 \times 10^{-6}$:

Sartorius of frog, Fenn (1928, 1 exp't. only)	7.1
Gastrocnemius, frog, Parnas (1921)	4.5
Meyerhof and Schulz (1927)	4.3

The mean for the seven researches on heart is $11.6 \cdot 10^{-6}$ cc. of oxygen. It is surprising to find that skeletal muscle uses less than half as much oxygen. As will be shown below, smooth muscle when its O_2 consumption is reduced to a similar basis appears to use $200 \cdot 10^{-6}$ cc., a figure nearly forty times more than that for gastrocnemius and nearly seventeen times more than that for heart muscle. An inaccurate tension factor could not be the cause of such great deviations. For if I allow 60 gram tension per gm. smooth muscle instead of 30, the O_2 used would still be nearly twenty times that used by gastrocnemius muscle.

The studies on carbohydrate metabolism in various mammalian heart muscles show no such great deviations. (For the literature see note 13.) Put in terms of gram carbohydrate used up per gm. muscle per gm. maximum tension exerted, I find the following (The figures in each case should be divided by 10^8):

Mammalian heart,—cat, Müller, 1904	0.88
rabbit, Locke and Rosenheim (1907)	0.43
cat, Rohde (1910)	1.00
dog, Knowlton and Starling (1912)	1.23
rabbit, Underhill and Prince (1914)	0.83
Mean of 5 investigations	0.87

Knowing now the ranges in the amounts of *carbohydrate used up* by mammalian heart muscle, one may calculate the O_2 required and compare the calculated with the observed quantities. This will be $0.87 \cdot 10^{-8} \cdot 1.92/180 = 0.93 \cdot 10^{-8}$ gm., or $6.5 \cdot 10^{-6}$ cc. of oxygen required, a number that is nearer the quantities observed for frogs' leg muscles and the two smallest observed quantities on heart muscle (*v. supra*) and is only a little more than one half of the mean value of all seven observed quantities of oxygen used by heart muscle.

The quantity of *carbohydrate mobilized during contraction*, while pretty well established for skeletal, has not been observed at all, to my knowledge, for cardiac muscle. One can only indirectly calculate the amount, and to do so may set out from the oxidation quotients known for skeletal, and as shown for smooth muscle when allowed to rest first in oxygen-want and then in oxygen-plenty. The quotient for smooth muscle as given by Evans (10) is 1/3.55. In studies on carbohydrate metabolism of frogs' gastrocnemius muscle Parnas (16) put the quotient at 1/4.0; Meyerhof and Schulz (12) at 1/4.7. (I calculate that the total carbohydrate mobilized by gastrocnemius muscle as observed by the former was $2.3 \cdot 10^{-8}$ gm.; as observed by the latter, $2.68 \cdot 10^{-8}$ gm. per gm. muscle and gm. tension.) The observed carbohydrate oxidized by heart muscle multiplied by the known oxidative quotients for different muscles then gives the quantities $2.92 \cdot 10^{-8}$, $3.49 \cdot 10^{-8}$ and $4.9 \cdot 10^{-8}$ gm.

respectively as possible quantities of carbohydrate mobilized during the systole. Let us assume that the middle figure, corresponding to Parnas' quotient 1/4, is the more nearly correct one. It may be stated then tentatively that during the beat there are $6.5 \cdot 10^{-6}$ cc., or $0.93 \cdot 10^{-8}$ gm., oxygen used and $3.49 \cdot 10^{-8}$ gm. carbohydrate mobilized. These numbers when multiplied by the Avogadro constant give $17.6 \cdot 10^{13}$ molecules oxygen, and $11.7 \cdot 10^{13}$ molecules carbohydrate respectively.

As will be shown later the anaërobic heat production as observed in the heart will require some correction. On page 86 of my paper (11) the total anoxidative heat is given as $3.2 \cdot 10^{-5}$ cal. For this I shall now subtract 1/5 which I believe is a fair estimate of the still uncorrected heat of oxidative origin. The proper oxidative heat given as the observed amount thus will be increased somewhat; in addition one must add the heat that is probably absorbed by synthesis of lactic acid into soluble glycogen. The revised figures are as follows in terms of microcalories:

Total "anoxidative" h.p. observed, 1928	32
1/5 to be deducted for O_2 leaks	6
Corrected total anoxidative h.p. observed	26
Total heat observed in oxygen, 1928	79
Corrected anoxidative heat	26
Corrected oxidative heat observed	53
Absorbed heat due to synthesis	15
Total heat of oxidative origin	68
Total heat produced per heart beat	94

The amount to be added as the heat absorbed during the resynthesis of carbohydrate is calculated from the oxidative quotient, $\frac{1}{4}$, and the carbohydrate mobilized. The amount synthesized theoretically being $\frac{3}{4}$ of the amount mobilized, we have $0.75 \cdot .87 \cdot 10^{-8}$ or $6.53 \cdot 10^{-8}$ gm., the heat equivalent of which must be $6.53 \cdot 10^{-8}$ (3836 − 3601) = $15.3 \cdot 10^{-6}$ cal.

Lundsgaard (Biochem. Zeit., 1930, *217*: 162) has just shown that muscle poisoned with mono-iodo-acetic acid is able to contract anaerobically without the production of lactic acid. Since E. Fischer (Die Naturwissenschaften, 1930, 18ter Jahrg. 736) has shown that the ratio of heat production to tension in anaerobic muscle poisoned with brom-acetic acid remains the same as has been found for normal anaërobic muscle, it would seem that some substance or substances other than lactic acid, but of equal calorific value are formed under the influence of the iodo-or Br-acetic acid. Lundsgaard has shown that the source of energy is probably in the breakdown of phosphogen.

The values put in terms of quanta are $26 \cdot 10^{-6} \cdot 4.19 \cdot 10^{7} / 18.65 \cdot 10^{-14}$, or *$5.85 \cdot 10^{15}$ quanta of anoxidative heat*, and $68 \cdot 10^{-6} \cdot 4.19 \cdot 10^{7} / 19.23 \cdot 10^{-14}$, or *$14.8 \cdot 10^{15}$ quanta of oxidative heat*.

Comparing with molecules in each case, the quanta yield is 585/11.7, or about *50 quanta per molecule of carbohydrate mobilized*, and 148/17.6, or about *8 quanta per molecule of oxygen used*, during the heart beat. If, instead of $6.5 \cdot 10^{-6}$ cc. oxygen as the observed volume used, we take the highest amount observed, namely $48.3 \cdot 10^{-6}$ cc. (Lüscher, on frog, 1920), then the ratio becomes *1.08 quantum per molecule of oxygen;* if the carbohydrate mobilized is the chemical equivalent of this amount of oxygen times the denominator of the 1/4.7 oxidation quotient, then the number of molecules mobilized is $10.2 \cdot 10^{14}$ and the quanta yield is 58.5/10.2 or *5.8 quanta of anoxidative heat for each molecule of carbohydrate.*

In other words only if one utilizes selected data on heart metabolism instead of the average of all data, does one find the law of equivalence valid for the oxidation process and the quanta yield for carbohy-

drate metabolism very similar to that for most other physiological processes (as exhibited in table 3).

2. The observed heat production and metabolic exchanges of contracting skeletal muscle

Passing on to skeletal muscle I may start with the initial heat production of frog's gastrocnemius muscle as observed by Snyder and Gemmill, 1925 (14). The mean of 31 observations on 6 different pairs of muscles stimulated through their nerves is $2.87 \cdot 10^{-5}$ calorie, the mean for the six different pairs irrespective of the number of observations on each pair is $2.83 \cdot 10^{-5}$ calorie. The mean temperature of these muscles was 8.32°C. The initial phase of heat production of the leg muscle of the frog is of comparatively very short duration and it is hard to imagine, even though enough oxygen is present, how oxidation could have time enough to add to the initial heat. However, when one recalls that silver atoms have been observed to orient themselves completely in a magnetic field in the brief period of 10^{-4} second (Stern and Gerlach) and that the time of exposure in the electric-spark photograph is no longer than one half millionth of a second, it would seem that a good deal of carbohydrate may combine with O_2 in say 0.1 of a second if the molecules are near each other at the outset. Moreover, in view of the great difference in initial heat observed in smooth muscle, —a difference of 66 per cent, when in .01 per cent oxygen compared with that when in .001 per cent oxygen (8), it will not be excessive in my opinion if we deduct one-third from the observed initial heat in gastrocnemius muscle, when in oxygen plenty, to get at the real anoxidative heat. This then will be $2.87 - 0.92$, or $1.95 \cdot 10^{-5}$ cal. The total observed heat production of unfatigued sartorius muscle in oxygen according to the latest revision by A. V. Hill (15) is 2.07 times the anaërobic heat. The ratio for gastrocnemius doubtless is the same and we may, therefore, conclude that the total heat production of this muscle is 2.07×1.95, or $4.04 \cdot 10^{-5}$ cal. The observable oxidative heat then is $4.04 - 1.95$, or $2.09 \cdot 10^{-5}$ cal. As shown above to this observable oxidative heat we must add the amount absorbed during the resynthesis of 3.7/4.7 of the mobilized carbohydrates, which is $2.68 \cdot 10^{-8} \times 3.7/4.7\ (3836\text{–}3601) = 0.45 \cdot 10^{-5}$ cal. The total heat of oxidative origin then is $2.09 + 0.45$, or $2.54 \cdot 10^{-5}$ cal.

The mean temperature of the gastrocnemius muscles was 8.32°C; $h\nu$, therefore, equals $19.1 \cdot 10^{-14}$ ergs. From this the heats as determined are: for the *anoxidative phase*, $1.95 \cdot 10^{-5} \cdot 4.19 \cdot 10^{7} / 19.1 \cdot 10^{-14}$, or *$4.28 \cdot 10^{15}$ quanta*; for the *oxidative phase*, $2.54 \cdot 10^{-5} \cdot 4.19 \cdot 10^{7} / 19.1 \cdot 10^{-14}$, or $5.56 \cdot 10^{15}$ quanta.

The carbohydrate mobilized by frog gastrocnemius muscle as determined by Meyerhof and Schulz (12, p. 568) is $2.68 \cdot 10^{-8}$ gm. per gm. muscle and gm. tension, if one divides their figures given in column 4, of Table 3 section C, by the corresponding tensions of the "a" muscles. The authors conclude that 1/4.7 of this carbohydrate was oxidized. The actual oxygen used by the muscles is also given by the authors, but for our purpose we may rely upon calculating back from the oxidation quotient. Thus there are $2.68 \cdot 10^{-8} \cdot 6.06 \cdot 10^{23} / 180$, or $0.9 \cdot 10^{14}$ molecules of carbohydrate mobilized; there being 6 O_2 molecules required for each molecule carbohydrate burned there will be then $6 \cdot 0.9 \cdot 10^{14} / 4.7$, or $1.15 \cdot 10^{14}$ molecules of oxygen. The quantum yield in each of these cases is: $4.28 \cdot 10^{15} / .09 \cdot 10^{15}$, or *47 quanta per molecule of carbohydrate mobilized* and $5.56 \cdot 10^{15} / .12 \cdot 10^{15}$, or *49 quanta per molecule of oxygen used by the muscle.*

For sartorius muscle of frog one may

start out from the data given by Hill and Hartree (1922) who observed the mean initial heat to be .0074 gm. cal. In view of the great avidity for oxygen that muscles show (8) we may subtract 1/3 from this number also and put .0074 − .0024, or .005 cal. as the initial heat of 1 gm. muscle. The tension exerted by 1 gm. of these sartorius muscles I find to have been 292 gm., hence the initial heat becomes $1.7 \cdot 10^{-5}$ cal. per gm. tension. The total heat (using the 2.07 ratio again) becomes $3.54 \cdot 10^{-5}$, and hence the observable oxidative heat 3.54 − 1.70 or $1.84 \cdot 10^{-5}$ cal. Adding to this the heat absorbed by synthesis we have 1.84 + 0.45, or $2.29 \cdot 10^{-5}$ as the total oxidative heat. These heats in terms of quanta (putting $h\nu$ at 1.5°C. *ca* the temperature of the observations) are $3.85 \cdot 10^{15}$ quanta of anoxidative heat and $5.14 \cdot 10^{15}$ quanta of oxidative heat, figures not greatly different from what were found above for the gastrocnemius muscle. Since the number of molecules engaged in sartorius contraction will have to be calculated from the same data used above for gastrocnemius the quantum yield will be only a little less, namely about *41 and 43 quanta* for *the two heats respectively*. On the other hand while the order of magnitude of quanta for the anoxidative phase is the same for both cardiac and skeletal muscle, it possibly differs for the oxidative phase of contraction, the quantum yield there just possibly obeying the equivalence law in the case at least of heart muscle.

3. *The observed heat production and metabolic exchange of contracting smooth muscle*

In a recent study of heat production of smooth muscle (8) it was shown that the total heat due to oxidation, per gram weight of muscle per gram tension exerted per contraction, has a value of $32 \cdot 10^{-6}$ calorie ($27.5 + 4.5 \cdot 10^{-6}$) for muscles in balanced breathing in an excess of oxygen. In the presence of an atmosphere containing less than .001 per cent oxygen the same muscles produced a total "anoxidative" heat of $11.6 \cdot 10^{-6}$ calorie. Again let us regard these heats as measures of effective radiant energies involved in the reactions. Then their quantities reduced to ergs and divided by the appropriate value of $h\nu$ will give the quanta required in each. The mean temperature of the experiments was 20.5°C with extreme variations ±1.8°C through the series. We, therefore, put $h\nu = 20 \cdot 10^{-14}$. The *oxidative process* in the muscle contraction thus has a value of $\frac{32.44 \cdot 10^{-6} \cdot 4.19 \cdot 10^{7}}{20 \cdot 10^{-14}}$, or $6.6 \cdot 10^{15}$ *quanta*, and the *anoxidative process* a value of $11.6 \cdot 10^{-6} \cdot 4.19 \cdot 10^{7} / 20\ 10^{-14}$, or $2.43 \cdot 10^{15}$ *quanta*.

From our knowledge of the chemistry of isolated muscle during activity there is almost conclusive evidence that not only skeletal but also smooth muscle in survival experiments oxidizes carbohydrate almost exclusively during the oxidative process. During the anoxidative process there is still much doubt as to what chemical changes go on, but whatever they are, the mobilization of carbohydrate into a substance of a calorific value equal to that of lactic acid seems to be by far the chief reaction, and, as was made probable in the paper just cited (8), may be the cause of the whole of the so-called anoxidative heat production. (Compare p. 294.)

No measurements of oxygen used or carbohydrate metabolism were made directly in the smooth muscles during the observations of heat production. Such determinations, however, have been made by others on smooth muscle as well as upon skeletal, and while it may seem farfetched to compare quantitatively results from other workers under somewhat different conditions, nevertheless the striking similarity I have found in the quantity of

heat produced by quite different smooth muscles when reduced to a common standard of comparison leaves little doubt that simultaneous direct metabolism determinations will likewise lead to a very similar result wherever done or upon whatever smooth muscle one chooses to study. For oxygen consumption we have the results of C. L. Evans (9, 1923) which, when reduced to a basis of 1 gm. muscle per hour I make out to be about 0.12 cc. at 20°C. Taking 30 gm. as the mean tension exerted in the contractions (10), we may say these smooth muscles used in three-minute periods (the probable time of a rhythmical contraction) $0.12 \cdot 3/60 \cdot 30$, or $2 \cdot 10^{-4}$ cc. per gm. muscle per gm. tension per contraction, which is equal to $2 \cdot 10^{-4} \cdot 1.429 \cdot 10^{-3} \cdot 6.06\ 10^{23}/32 = 5.4 \cdot 10^{15}$ molecules of oxygen.

The energy of the anoxidative processes of smooth muscle contraction, we may assume, comes from the breakdown of carbohydrate into lactic acid, direct evidence for which is given by Evans (10), who further concludes (p. 389) that 1/3.35 part of the lactic acid formed during the muscle action is oxidized completely while the rest, as in skeletal muscle, is resynthesized back to glycogen. The oxygen consumed in the smooth muscle action being already given, one may calculate back to the total amount of soluble carbohydrate probably mobilized in the reaction, that is, following the physiological stimulus. Thus, since six molecules of oxygen are required in oxidizing one molecule of carbohydrate, we have the ratio $6{:}1 :: 5.4 \cdot 10^{15} : X$. Since the ratio of oxidized to mobilized is 1/3.35, then $3.35X = 3.0 \cdot 10^{15}$ molecules, the total *mobilized carbohydrate*. As shown above there were $2.43 \cdot 10^{15}$ quanta of heat liberated in the anoxidative process. *The ratio of molecules to quanta*, therefore, is $3.0 \cdot 10^{15}/2.43 \cdot 10^{15}$, the quotient of which is 1.24. It would seem that the number of molecules to the quanta of heat engaged in the chief reaction of the anoxidative phase of smooth muscle contraction is not far from unity.

It was shown that the number of molecules of oxygen required in the oxidative process is $5.4 \cdot 10^{15}$ and the corresponding oxidative heat quanta, $6.6 \cdot 10^{15}$. The ratio of molecules of oxygen to quanta thus is 5.4/6.6, the quotient of which is 0.82. If the molecules of carbohydrate and oxygen are added together and their total number divided by the sum of anoxidative and oxidative quanta then we have a ratio of 8.4/9.03, or 0.93 molecules of both kinds per quantum of heat.

4. The value of the effective frequency as calculated from the observed data on smooth muscle and as demanded by Wien's law of displacement and Einstein's law of equivalence

Another way of comparing our experimental data with the radiation hypothesis of energy exchanges, as stated in the introduction of this essay, is to apply Wien's law of displacement directly. Let us assume that the data indicate that the equation for equivalence holds for the process of smooth muscle contraction, that is $q/Nh = 1$. Then it follows that $\nu = q/Nh$, where the sum of the mean heats observed for oxidative and anoxidative phases, namely $43.6 \cdot 10^{-6}$ calorie, may be substituted for q in terms of ergs, and the sum of the mean number of oxygen molecules and molecules of carbohydrate mobilized may be substituted for N, namely $8.14 \cdot 10^{15}$ molecules. Then,

$$\nu = \frac{43.6 \cdot 10^{-6}\ 4.19 \cdot 10^{7}}{8.4 \cdot 10^{15} \cdot 6.55 \cdot 10^{-27}} = 3.3 \cdot 10^{13}$$

which is the frequency of the effective radiant energy. Since the frequency is a function of the wave length, and since according to Wien's law, $\lambda\mu T = 2882$, we

are able to calculate the mean temperature at which the muscles functioned. For it is obvious that given $\lambda = C/\nu$, Wien's equation may be written, $T = 2882\nu/C$. In solving for T the velocity of light, C, is put in terms of μ/sec. and the frequency of the effective radiant energy found above is substituted for ν; whence $T = 2882 \cdot 3.33 \cdot 10^{13}/(3 \cdot 10^{14}) = 319.9$ degrees absolute. Now the mean temperature of the smooth muscles in the heat-production determinations, as stated above, was 20.5°C ± 1.8. In terms of the absolute scale this is 273.2 + 20.5, or 293.7 degrees, a figure that is 8.2 percent less than the figure required by theory, but even so in much closer agreement than usually obtains among physiological processes.

5. *Summary and discussion of the findings of Chapter III*

Summing up the results of the inquiry thus far made on muscle in balanced breathing and in a unit of physiological action, we may say, on the radiation hypothesis of chemical activation, that (a) For smooth muscle about 1.2 molecule of carbohydrate appears to be mobilized per quantum of observed anoxidative heat, and about 0.8 molecule of oxygen is used per quantum of observed oxidative heat; or that about 0.93 molecule of the total carbohydrate and oxygen is engaged per quantum of the total observed heat production. (b) For heart muscle it may be that from 6 to 50 quanta of heat energy are required per molecule of carbohydrate mobilized, and from 1 to 8 quanta per molecule of oxygen used. (c) For skeletal muscle in a complete contraction-recovery from 41 to 47 quanta of anoxidative heat appear per molecule of carbohydrate mobilized and from 43 to 49 quanta per molecule of oxygen used.

The close agreement, in the case of smooth muscle, with the law of equivalence, however remarkable, can not as yet be considered established. For the data upon which the calculations are based as to oxygen and carbohydrate metabolism are all too meagre. Nor may we hope that additional metabolism investigations of the kind that have been lavished upon heart muscle in the past, if once directed toward smooth muscle, will lead to more certain conclusions. As for the heart muscle, although one or two observations meet the demands of the law of equivalence, many others do not. The discrepancy seems to lie among the observations of the chemical changes, the amount of carbohydrate mobilized not having been observed at all. The observations of carbohydrate and oxygen used by the heart vary greatly even after reducing them to a common basis of comparison. The lower quanta-yields for the heart muscle are more nearly equal to the quanta-yield found for many other physiological processes. The great divergence of observations in heart muscle appears to be due in large part also to lack of uniformity of experimental conditions, and the want of a common standard for measurement. To measure the chemical changes occurring in hearts during unit time has no sense whatever. A unit of physiological response should be made the basis; at least the number of these units should be observed along with the time units.

As for the observations on skeletal muscle, it would seem that the above criticism would not apply so justly. In recent years much accurate work has been done on these muscles, the unit of physiological response being kept well in mind. But it is just here that quanta yield also indicates that the law of equivalence does not apply. Whether later it can be shown that the law holds for the primary reaction, and just what that

primary reaction may be, cannot now be stated. In passing it may be pointed out that the quanta relations in skeletal muscle remind one of the finding of E. Newton Harvey (2) in his work on the luminiferous material extracted from the crustacean, *Cypridina*. Only the quantum yield here appears to be just the reverse; instead of an excess of quanta Harvey finds an excess of molecules, at least 50 molecules of oxygen being required for each quantum of light emitted by the luciferin + O_2 reaction.

IV

RELATION OF ENERGY AND IONIC EXCHANGES IN PHYSIOLOGICAL STIMULATION

Physiological stimulation has already been considered in part in the chapter dealing with rhythmical processes. For the rate of spontaneous rhythms, within limits, *is determined* by *the rate of development of the inner stimuli*. As we have seen (see the summary, p. 291) the $q/Nh\nu$ value of the processes examined lies between 4 and 7. In this chapter it is proposed to deal briefly with external stimuli, inadequate and adequate, that may be applied to nerve and sense organs.

Whenever the energy of the effective stimulus can be measured then the relation between that energy in terms of quanta and its effect in terms of the number of molecules or ions made reactive may be estimated. Indeed, whatever the outcome of such a study may be, one positive result should be gained, namely, a more definite idea as to the relative number of molecules or ions probably made reactive at the point of the effective stimulus and hence the number necessary to set up a nervous impulse.

The difficulty of making a correct estimate of quantum relations and stimulating intensities appears at once when one considers that most stimuli fall on indifferent tissues as well as the particular tissue one wishes to stimulate. Electrical currents applied to nerve-trunks must traverse intervening connective tissue, myelin sheaths, intercellular fluid, etc., before reaching the axons; all of whose resistances, and, therefore, whose share of current, we have little chance of knowing. For the same reason adequate stimuli are difficult to evaluate quantitatively. In selecting data from the literature, therefore, care must be taken to select only those where excess energy as well as the loss of exciting energy has been taken into account. Let us begin with a consideration of stimulations that are quite obviously of the radiational type.

1. The probable number of molecules or ions made reactive by a least effective electrical stimulus

We may begin with an example of artificial or inadequate stimulation, the commonly used electrical stimulus. This has all the objections just mentioned. A strength of current equal to that of the natural bioelectric current is known to be intensive enough to act as a stimulus to other tissue, as is exemplified in the classical rheoscopic frog. Among the estimates of the absolute value of the energy exchange in the passage of an action current we have those of A. V. Hill (17). Basing his calculation upon the observed E.M.F. and duration of the action current, and the resistance offered by the tissue traversed, Hill concluded that the energy value of a single action potential wave traversing 1 gm. of muscle, whose fibers are 1 cm. long, is about $23.9 \cdot 10^{-9}$ calorie at 8°C and $6.6 \cdot 10^{-9}$ calorie at 18°C; and the energy value of a single wave passing through 1 gm. of nerve fibers 1 cm. long is about $3.5 \cdot 10^{-10}$ calorie at 6.2°C. In what follows we shall call these the "observed" energies.

From the formula (see chapter I),

$$\lambda_{\mu} = 6.35/T\,(T + 10) \log Q_{10},$$

one determines the radiation frequency. The energies given at the two temperatures indicate that Q_{10} is 3.55 for the case of muscle, whence the wave length will be $6.35/281 \cdot 291 \cdot \log 3.55 = 1.41\mu$. The frequency corresponding to this wave length is $2.12 \cdot 10^{13}$, one that lies well within the region of the infra-red, and above the electro-magnetic frequencies, as one may have expected of an electrical action potential. The mean of the observed energies (in the case of muscle $15 \cdot 10^{-9}$ cal.) divided by $h\nu$ will give us the energies in terms of quanta. Thus for muscle $\frac{15 \cdot 10^{-9} \cdot 4.19 \cdot 10^{7}}{6.55 \cdot 10^{-27} \cdot 2.12 \cdot 10^{13}} = 4.4 \cdot 10^{11}$ quanta. If we assume further that the law of equivalence holds in these cases then the number of molecules or ions made reactive in the muscle is equal to the quanta engaged, that is, also equal to $4.4 \cdot 10^{11}$. And if the solvent for these ions occupies, say, one-tenth of the gram muscle (in all probability it cannot occupy the whole of the muscle substance) then the concentration of the ions will be about $4.4 \cdot 10^{11}/6.06 \cdot 10^{19}$ or $7.2 \cdot 10^{-9}$ of a gm.-mol. solution.

One may also calculate the effective radiation frequency directly from the observed temperature and Wien's displacement law, and finally the value of one quantum. This into the observed energy of the action current again gives the energy in terms of quanta. The operation is all included in the equation, $q/h\nu = q/h\,(cT/.2882)$, where again c is the velocity of radiant energy, T the absolute temperature and h Planck's constant; the numeral is the constant in Wien's law. Substituting with the observed data given above one finds that for the action current of muscle at 18°C., $q = 14 \cdot 10^{11}$; at 8°, $q = 5.1 \cdot 10^{12}$ quanta. The energy for the action current of nerve at 6.2°C., by the same calculation is equal to $7.75 \cdot 10^{12}$ quanta.

If we again assume that Einstein's law of equivalence holds in the case of bioelectric currents then we can further calculate the probable concentration of the ions made reactive, since then, for every quantum a molecule or ion is made reactive and the total number in each case equals the number of quanta. We assumed that only 0.1 of the mass of tissue held the ions affected in solution. The total number in a gm. mol. solution of 1 gm. nerve or muscle then may be put at $6.06 \cdot 10^{19}$ The quanta in each case given above divided by this number show the concentrations to be $2.3 \cdot 10^{-8}$ and $8.4 \cdot 10^{-8}$ gm.-mol. for the muscle at 18 and 8 degrees respectively, and $1/3 \cdot 10^{-7}$ gm.-mol. for the nerve fibers at 6.2 degrees.

Recalling that the concentration of the hydrogen ions in the purest water gives about an $8.5 \cdot 10^{-8}$ gm.-mol. solution, it appears that the concentration of the ions made reactive, as the intenser waves of the electrical action potential sweep over muscle or nerve, is probably no greater than the concentration of those ions in pure water.

2. *The probable number of molecules or ions made reactive in the retinal elements by a minimal effective light stimulus*

Of all forms of stimulation the absolute quantity of light falling on the retina is probably most accurately estimated and hence data from this field of observation are probably best suited for our present purpose.

Of several measurements by different workers as to the minimal light energy necessary to produce a retinal perception one may take those of von Kries and Eyster (18). It will be recalled that in

these experiments the light used was of a mean wave-length, 507 mμ, the part of the spectrum that had already been shown to be most effective for the dark-adapted human retina. The minimal light energy required to produce a retinal perception under optimal spatial and temporal conditions (time exposure of about 1/8 seconds) was calculated by von Kries to be from 1.3 to $2.6 \cdot 10^{-10}$ ergs. Correcting for probable refractory periods, however, requires a reduction by one-eighth, or to a mean of $2.3 \cdot 10^{-10}$ ergs, as the energy actually made effective.

If we assume that the law of equivalence holds in the photochemical reaction taking place in the retina then we may calculate the number of molecules made reactive in the rods. Light of wave length 507mμ has a quantum value of $6.55 \cdot 10^{-27} \cdot 5.9 \cdot 10^{14} = 3.86 \cdot 10^{-12}$ ergs per molecule. The total number of quanta, and therefore molecules, required to absorb the whole of the energy would then be $229.10^{-12}/3.86 \cdot 10^{-12}$, or about 60 molecules.

There is probably a refractory period following every excitation wave set up by the retinal cells. The time of this is not known but it is this factor that determines rhythm rate. By taking one of the higher normal rhythm rates known for excitation waves multiplied by one of the briefer known chronaxie rates we may get a rough measure of the probable time during which the cells are absorbing light. A rhythm rate of 125 times a chronaxie of .001 second indicates a period of 0.125 second out of every second during which the light reaction is being reversed. The effective part of the energy thus becomes only about 7/8 of the total energy of the incident light, or about $2.3 \cdot 10^{-10}$ ergs, and the probable number of molecules made reactive is again nearly 60.

The interested reader may compare this result with that of Noddack (22), who calculates that only 30 $h\nu$ or light energy incident upon the eye is required for a minimal visual stimulus; and, assuming that 29/30 of this is ineffectual, concludes that only 1 $h\nu$ is utilized in the actual retinal stimulus.

It now becomes a matter of further interest to know the approximate concentration of these 60 molecules. Although the data and method of calculation are given in his paper, von Kries does not state the exact areas of the retina illuminated. There is good evidence that the smallest area that can be stimulated, and still give a light perception, must include at least two rods. In the human retina these elements are about 2μ in diameter and 60μ long, and only their outer halves are said to contain the visual purple. The volume contents of these two outer halves being the same as that of one rod, the volume becomes $\pi r^2 h$, or 188 μ^3. It is hardly likely that the whole of even this small volume is filled with a solvent for the specific light sensitive substance; let us suppose it occupies 1/100 of the volume, then the volume holding the 60 molecules becomes only 1.88μ^3. Since now a gram-molecular solution filling this space requires that $6.06 \cdot 10^{23} \cdot 1.88/1.10^9$ or $1.14 \cdot 10^{15}$ molecules are in solution, the concentration represented by the 60 reactive molecules must be $60/1.14 \cdot 10^{-15}$, or about a $5.5 \cdot 10^{-14}$ gm. mol. solution. The area of the retina stimulated, however, having been an *optimal* area for a minimal stimulating strength, probably was somewhat larger than the one just considered; but the number of molecules according to our postulate remains the same, and, therefore, their concentration even less than the concentration indicated when only two rods are stimulated. For example, if 400 rods instead of two were stimulated

then the concentration would be a $2.7 \cdot 10^{-16}$ gm.-mol. solution. If the case of two rods only be considered then the concentration of hydrogen ions in the purest water appears to be $(8.5 \cdot 10^{-8}/5.5 \cdot 10^{-14})$, nearly $1.5 \cdot 10^{6}$ greater than highest probable concentration of the reactive photochemical substance in the retina when stimulated by the least amount of energy capable of evoking a light perception.

The work of Boswell (19) on the minimal light energy falling on the fovea, required to produce a visual perception, gives the desired data somewhat more precisely. The observations were also made in von Kries's laboratory and with nearly the same method and apparatus that Eyster used for the study of peripheral vision. I choose the data obtained with the sodium flame, maximal energy in wave length of 589 $m\mu$; frequency, $5.1 \cdot 10^{14}$. The minimal area illuminated in four series of observations of different durations appears to have been .00361 mm. in diameter, the mean duration of the stimulus .0061 second.

The cones in the human fovea are known to be about 2μ in diameter by 34μ in length. The illuminated area divided by the area of one cone, or r^2 of the one area by the r^2 of the other, will give the number of cones covered by the incident light. This gives in this case 1.8 cones whose total volume is $1.8 \cdot 1^2 \cdot \pi \cdot 34 = 192\mu^3$. Assuming in the case of the cones the solvent for the photochemical substances occupies only 1/10 of this volume, we have $19.2\mu^3$ in which the molecules or ions are dissolved.

Boswell calculated the energy of the light absorbed by the fovea in the above cases to have a mean value of $31.6 \cdot 10^{-10}$ ergs; allowing for probable refractory periods this should be reduced 1/8, that is $27.6 \cdot 10^{-10}$ ergs. The quantum value of wave length employed is $6.55 \cdot 10^{-27} \cdot 5.1 \cdot 10^{14} = 33.4 \cdot 10^{-13}$ ergs per molecule, in the case that the law of equivalence holds; whence $27.6 \cdot 10^{-10}/33.4 \cdot 10^{-13} = 826$ molecules appear to have been made reactive. In this case the concentration of the molecules if dissolved in the volume allowed above will be $826/19.2 \cdot 10^{-9} \cdot 6.06 \cdot 10^{23} = 71 \cdot 10^{-15}$ of a gm.-mol. solution, a concentration that is about 1.2 million times more dilute than the hydrogen ions in purest water. The probable concentration of reactive ions in the two cases (of cones and rods) thus turns out to be very nearly the same, however incredibly dilute this concentration appears to be.

3. Quantum yield in the reduced latent time of a light stimulus as affected by dark adaptation

In the cases of retinal stimulation just considered I assumed that the law of equivalence was valid, the necessary data to make a quantum yield determination not being available. There are, however, other investigations of sensory mechanisms that give us data for such determination in their respective fields.

It is known that among certain animals the reaction time to a photic stimulus diminishes as dark-adaptation proceeds, and only approaches a constant as this process reaches completion (20). If one subtracts from the gross reaction time that time necessary for the excitation, when once set up, to travel over the reflex arc, then the remaining time must be due to processes going on only in the photoreceptors, a period of time that may be called appropriately the reduced latent time of light stimulation as influenced by dark-adaptation. By observing further the influence of temperature changes on this reduced latent time one obtains a temperature coefficient and may then calculate the reactivity constant, q, the

radiation frequency and finally its quantum value. In his study on influence of temperature upon latent period of dark adaptation Hecht (20) has found that for *Mya arenaria*, q = 19,700 cal., between 11.5 and 21.9 degrees C., and for *Pholas dactylus*, q = 18,300 cal., between 10.5 and 18.4 degrees C. The quantum yield for *Mya*, $q \cdot 4.19 \cdot 10^7 / Nh(CT).2882$, is 6.9 per molecule and for *Pholas* 6.45 per molecule.

4. The quantum yield in the absolute refractory period of nerve stimulation

In all cases of stimuli repeated at intervals sufficiently close there appears the phenomenon known as refractory state. On page 181 of my 1908 paper (7) I pointed out that the observations of Gotch and Burch showed that the refractory period of frog's nerve had a temperature coefficient of about 3.6. Amberson (21) just lately has reinvestigated the phenomenon, confining his attention to the absolute refractory period and using as end-point the least interval required for the appearance of a second electrical response, "which is not further shortened by a considerable increase in the magnitude of the second stimulus." The plotted results "outline a curve which is approximately exponential in form," with a Q_{10} value of 3.06 between 27 and 9 degrees C. Using Amberson's temperature coefficient the energy increment, q = log $Q_{10} \cdot .457 \cdot 300 \cdot 281 \cdot 4.19 \cdot 10^7$ = $7.62 \cdot 10^{11}$ ergs per gm.-mol. The frequency at median temperature is $C \cdot 291/.2882 = 3.03 \cdot 10^{13}$. Whence, $q/Nh\nu = 7.62 \cdot 10^{11}/Nh \cdot 3 \cdot 10^{13} = 6.25$ quanta per ion, or molecule of the substance made reactive during the absolute refractory period of frog's sciatic nerve.

Thus, for the latent time of dark adaptation and for refractory period of nerve fiber the quanta yield appears to be near the mean found for the many cases listed in the table at the end of Chapter II. If this quantum yield is also true for minimal retinal stimulation, then the concentrations of molecules or ions taking part in the setting up of that stimulus will be from 3 to 10 times that calculated above, a figure which still leaves the concentration some 2 to 6 million times more dilute than hydrions in purest water.

V

CONCLUSION

The results of the foregoing inquiry are of the kind that clearly indicates the need of further investigations carefully planned and directed towards the determination, as precisely as possible,

(1) As to what constitutes the most elemental response, and recovery therefrom, in living matter when given an adequate stimulus. This may be called the unit of physiological action.

(2) The energy and chemical exchanges, their nature and quantitative relations, at least in the initial and final stages of this unit of physiological action.

(3) The character, quantity and fate of the energy making up the adequate stimulus evoking the unit of physiological action. What part of the energy of such stimulus is lost in the transfer to the effective points in the responsive tissues, what part of it becomes effective?

Indeed may it not be that in the end we shall find that all adequate stimuli at the moment they reach the site of final action are no more nor less than one form or another of radiant energy, and that they evoke responses in living matter in the same manner as light initiates a photochemical reaction in the test-tube, and that the molecules only become "reactive" when the energy they absorb has reached a certain critical value limited by the frequency of the radiation? Indeed the old

Weber-Fechner Law of stimulation could have no more reasonable physical basis. Our perception of increasing stimulating-strength occurs in jumps because the unit of physiological action required at least one quantum of energy to evoke a response.

And yet,—when once this critical difference in frequency has been shown to exist it may well be that the story of quantum relations to non-luminous physiological reactions will turn out much the same way as has the story of photochemical reactions. It may be that only now and then the law of equivalence will be found to hold good, and that as in the purely photo-chemical reactions primary and secondary or even "chain reactions" will have to be invoked to explain the many cases where the law finds no direct application. But if this relation between a clean physiological action and the quantum theorem can be established thoroughly in a single case there will be revealed a control of the forces of life by the most universal of all the known laws of nature.

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CONSTANTS AND SYMBOLS USED IN THIS PAPER

c = 2.9986.10^{10} cm/sec, velocity of radiant waves

h = 6.556.10^{-27} ergs/sec, the Planck radiation constant

N = 6.061.10^{23}, molecules per gm. mol. wt.

R = 8.315.10^{7} ergs/deg. per gm. mol. wt. or 1.985 cal/deg. per gm. mol. wt.

C_2 = 1.4300 (radiation constant of Holborn-Valentiner, E. Warburg, etc.) = Nhc/R

$q = \mu = 2a$, heat of activation in the Arrhenius equation for temperature reaction velocities.

ν = rate of vibration of radiant energy

ρ = Perrin's "universal constant" as used in his "Matière et lumière," p. 20 ff.

$\rho = \frac{1}{2.1}.10^{-10}$, and is derived as follows: In the Arrhenius equation, $k = se^{-\frac{a}{T}}$, a is put equal to $\rho\nu$; but since a also $= q/R$, $q = aR$. The radiation hypothesis of chemical reaction puts $aR = Nh\nu$, from which $a = \frac{Nh}{R}.\nu = \rho\nu$, whence $\rho = \frac{Nh}{R} = \frac{1}{2.095}.10^{-10}$, a ratio without dimensions.

UNISEXUAL PROGENIES AND SEX DETERMINATION IN SCIARA

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TWO apparently distinct types of reproduction are found in the genus *Sciara*, as indicated by sex ratios. In the one type, which may be designated "digenic," bisexual progenies are produced. In the other, or "monogenic" type, the progenies are essentially unisexual. I am indebted to Prof. E. B. Wilson for suggesting these terms. Different species of the genus appear to differ in respect to mode of reproduction. In some species reproduction is characteristically digenic, in others characteristically monogenic, and in others both types are found. Six species have been studied rather extensively and seven others slightly. The six best known species are divided equally among the three classes on the basis of progenies obtained from wild females.

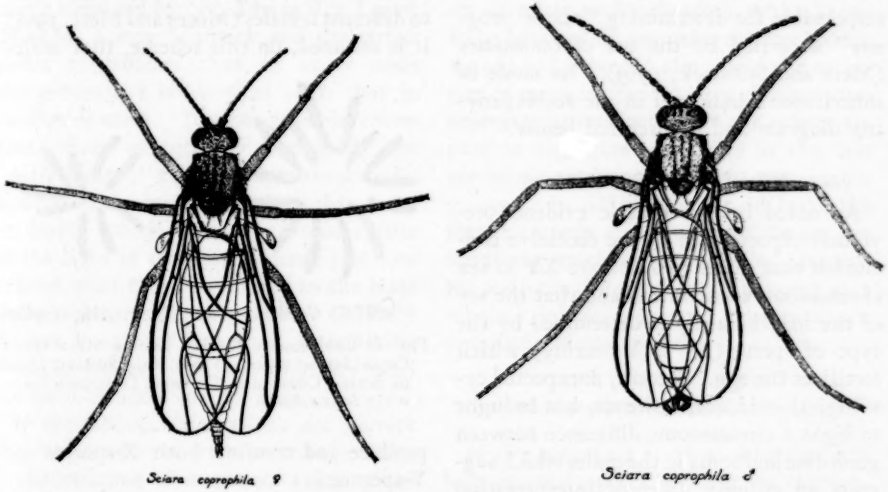
The fact that two species include strains of both kinds suggests that possibly the other species would reveal both types frequently if sufficient material were secured in nature. This is opposed, however, by the fact that each of the three best known species has been definitely of one type or the other—two monogenic and one digenic. Geographic distribution, so far as observed, is not a factor of importance in this connection. In the case of the three species just mentioned collections have been made in several localities including the northeastern and the southwestern parts of the United States, with uniform results throughout. In the case of the two species giving both types of sex ratios, on the other hand, the two types were secured from flies taken in the same localities. Within any one species no morphological difference has been detected between individuals or strains of the monogenic type and those of the digenic type, and the two kinds have proved interfertile in crosses.

Among the seven species in which relatively few wild specimens have been secured, five are of the monogenic type and two of the digenic. Apparently the monogenic mode of reproduction is the more widespread in the genus, at least as regards American species.

The most noteworthy feature about the sex ratios in the digenic forms is the fact that the proportions of the two sexes vary widely in different progenies instead of conforming to a 1:1 ratio. It is possible that the divergence here is due to differential viability, together with the fact that males emerge before females, on the average; but the evidence weighs strongly against this interpretation. (Details regarding this and other features are to be considered in another paper.) It appears more probable that the ratios here are not modifications of a fundamental 1:1 ratio, but are modifications of the basic 0:1 and 1:0 types found in the monogenic forms. This feature will be considered further below.

On the other hand, it is not to be concluded that the monogenic and digenic types of reproduction are alike and that the distinction made here is purely artificial. The constancy of the distinction between the two has been shown clearly by study of representative species such as *S. coprophila* Lint., and *S. impatiens* Johan., both of which are typically monogenic, and *S. pauciseta* Felt, which is digenic. In all three of these species progenies have been obtained from many wild females and from many generations of pair matings in the laboratory. Whereas, in the former two species the progenies have been almost exclusively of the "unisexual" type, those in the last species have been consistently of the bisexual type. Furthermore, in both *S. coprophila* and *S. impatiens*, the species studied most extensively, an "exception which proves the rule" has been secured in the form of a digenic strain. That in *S. coprophila* was derived in the laboratory from a pedigreed inbred monogenic strain. This digenic strain descended from a single female and its digenic characteristic has been shown by crosses to be due to a genetic modification distinguishing it from the regular monogenic type. The digenic strain in *S. impatiens* was derived from one wild female and showed the same type of genetic differences from the monogenic strains as did that in *S. coprophila* (unpublished data).

Most of our work has been devoted to a study of the monogenic type of reproduction, using especially *S. coprophila*, and to a lesser extent *S. impatiens*, as material. The following résumé includes the main results of this study up to the present time.



SCIARA COPROPHILA LINTNER. Camera drawings of wild-type female and male; not at same magnification. Actually the female is considerably larger than the male.

SEX OF PROGENY

In considering sex determination in the broad sense it is necessary at the outset to distinguish between the determination of the sex of the progeny as a whole and that of the individual fly. The sex of the progeny has been shown (Moses and Metz, 1928) to be due to the zygotic constitution

of the female. Female-producing females and male-producing females are ordinarily present in equal numbers in female progenies, showing that the mother is heterozygous for some factor which distinguishes between the two types (Metz and Moses, 1928). Present evidence, although not complete, indicates also that it is the zygotic constitution of the female which makes the distinction between monogenic and digenic modes of reproduction. Genetic studies with the aid of mutant characters have shown that the differential responsible for determining "sex of progeny" is carried by the sex chromosomes (Metz and Schmuck, 1929). Its mode of inheritance is indicated in the accompanying diagram and is discussed below.

SEX OF THE INDIVIDUAL

As noted below, genetic evidence previously reported led to the tentative conclusion that males in *Sciara* are XY in sex chromosome constitution and that the sex of the individual fly is determined by the type of sperm (X- or Y-bearing) which fertilizes the egg. Recent, unexpected cytological evidence, however, has brought to light a chromosome difference between germ-line and soma in the males which suggests an entirely different interpretation of this process. Owing to the fact that neither the genetic nor the cytological line of evidence is complete, as yet, both are reviewed briefly, together with the possible interpretations which they suggest.

(1) Genetic evidence

The genetic studies already mentioned (see also Metz and Ullian, 1929) reveal the presence in these flies of sex linked inheritance of the type commonly found where the female is XX and the male XY in constitution. It would seem to follow, therefore, that such sex chromosomes are present, although they have not been distinguished cytologically. The presence of Y is inferred from the fact that in males (spermatogonia) the chromosomes are present in pairs. With females essentially XX and males XY in constitution it would likewise follow that the sex of the individual is "determined" by its sex-chromosome constitution, which presumably is in turn determined by the type of sperm (X-bearing or Y-bearing) fertilizing the egg.

Since individual males will give offspring of both sexes in large numbers, when mated to different females (Moses and Metz, 1928) it is assumed, on this scheme, that males

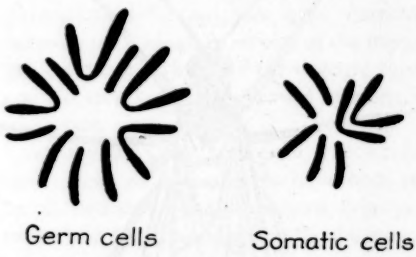


FIG. 1. CHROMOSOME GROUPS IN THE MALE GERM CELLS (SPERMATOGONIA) AND MALE SOMATIC CELLS OF SCIARA COPROPHILA LINTNER; DRAWINGS SOMEWHAT SCHEMATIZED

produce and transmit both X-sperms and Y-sperms.

(2) Cytological evidence. Chromosomal differences between soma and germ-line in males

The evidence in this section has been secured entirely from *Sciara coprophila*, Lintner. In former papers it has been stated that in this species the male chromosome group (diploid) includes either ten or nine chromosomes and the female group eight. These counts were made from spermatogonia and spermatocytes in the one case and ovarian cells (probably all follicle cells) in the other. The male group, as described, includes eight chromo-

somes like those in the female, and in addition two (sometimes only one) much larger "male-limited" chromosomes (Fig. 1). Recent examination of somatic tissues in the males of this species indicates that the soma possesses only seven chromosomes—the two "male-limited" chromosomes and one of the rod-like "ordinary" chromosome being absent (Fig. 1). An attempt has been made to complete the comparison by examining the chromosomes in the female germ-line, but without complete success, as yet. Evidence obtained by Mr. Adrian Ter Louw, Miss M. Louise Schmuck and the writer seems to indicate that in many cases the group here is identical with that in the female soma. It seems possible, therefore, that, as formerly supposed, the "male-limited" chromosomes are actually limited to the males, although this is by no means certain. If so, it would appear in the light of the new evidence just considered, that they are limited to the male germ track. Since they almost certainly do not have any direct sex determining function (Metz, 1929, *loc. cit.*) they need not be considered further here.

If the above observations are correct they require the assumption that in males a chromosome elimination takes place from somatic cells (presumably during cleavage) removing the "male-limited" chromosomes and one of the ordinary chromosomes. It seems probable that this process is in some way connected with sex determination and that the "ordinary" chromosome which is eliminated is a sex chromosome. Should this be the case, then two possibilities are presented: If the male is XY in sex chromosome constitution, the Y is evidently regularly eliminated. On the other hand, it is possible, as first suggested to me by my colleague Dr. M. Demerec, that the sex chromosomes of the male are both X-chromosomes and that the sex of the individual male is "determined" by the elimination of one X from the soma, regardless of the fact that the germ-line (*Keimbahn*) would possess two. Should this be the case, then it is clear from the evidence of sex linkage mentioned above, that it is regularly the paternal X which is eliminated.

Although there is no direct evidence, as yet, in favor of the latter hypothesis, it has the advantage of simplicity. It would avoid the necessity of assuming a process of selective fertilization, which seems to be required by any other scheme (Metz, 1929a) and it would also avoid the necessity of assuming that the sex chromosomes segregate at random while the others appear to segregate selectively at the first spermatocyte division (Metz, 1926, 1929b, p. 492). In addition it would leave the female entirely responsible for the sex determining mechanism, both as regards the individual fly and the "progeny as a whole" where unisexual progenies are obtained (Metz, 1929b).

THE MECHANISM OF SEX DETERMINATION

In the preceding section attention has been devoted especially to the sex chromosomes of the male, showing that, with present evidence, either one of two distinct conditions might exist, depending on whether sex in the male is determined by the process of chromosome elimination just considered, or in the ordinary fashion by the union of a Y-bearing sperm and an X-bearing egg.

Turning to conditions in the female we find much less uncertainty, both as regards the individual fly and the progeny which she produces. From the considerations indicated above (regardless of which of the two alternatives is correct) it appears that the sex of the individual female and

the sex of the progeny as a whole are both "determined" by the same pair of chromosomes—the sex chromosomes. It also appears that the two types of females (male-producing and female-producing) differ in respect to sex chromosome constitution. Genetic evidence has shown (Metz and Schmuck, 1929; Metz, 1929) that in the male-producing female both sex chromosomes are like the X-chromosome of the male, but that in the female-producing female only one is strictly of this kind, the other differing in respect to the differential responsible for "sex of progeny."

This latter chromosome, designated X′ to distinguish it from the X, is ordinarily limited, of course, to the one class of females, and does not regularly pass back and forth between females and males as does the X. For the most part, however, it apparently resembles the X in constitution (see below).

On the basis of these observations the scheme shown in the accompanying diagram (Fig. 2) has been proposed as an interpretation of sex chromosome behavior here. So far as the sex chromosomes of the female are concerned this scheme accounts for all the facts thus far observed. Furthermore, it has been subjected to two critical tests which, in our opinion, establish it as essentially correct, *as regards the female*. The tests concern the constitution of "exceptional" individuals which appear frequently in "unisexual" progenies. As pointed out in earlier papers (*l.c.*) the "unisexual" progenies in *Sciara* are not exclusively unisexual. A few males occasionally appear in female progenies and a few females in male progenies. Such individuals are designated "exceptions." It is evident from the diagram that "exceptional" males in female progenies should be of two kinds, X (Y?) and X′ (Y?). The former should be like ordinary males in constitution and should exhibit the same genetic behavior. The latter, however, should differ and give different results in crosses, due to the presence of X′. When crossed with female-producing females their daughters should all be female-producers, and half of these should in turn give only female-producing daughters. These expectations have been verified by the results (Metz and Schmuck, 1929-b). On the same principle exceptional females in ordinary male progenies should all be of one kind, male producers, because neither parent would contribute an X′ chromosome. Here again the expectation has been confirmed (Metz and Moses, 1928).

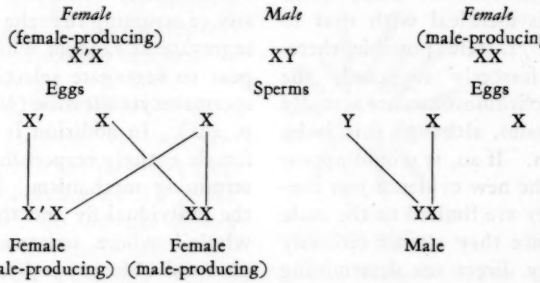


FIG. 2. DIAGRAM ILLUSTRATING SEX CHROMOSOME MECHANISM IN SCIARA COPROPHILA

This scheme is especially designed to represent the sex chromosome constitution of the females. As explained in the text the constitution of the male germ-line is as yet uncertain. It may be like that of the male-producing female (XX). In either case the male soma is presumably XO in make up.

THE NATURE OF THE X′ CHROMOSOME

Since the evidence indicates that the X′ chromosome differs from the ordinary X chromosome in these flies, it is of especial interest to ascertain the exact nature of this difference. The data are as yet insufficient for the purpose, but they reveal some features of significance (Metz and Schmuck, 1929). It has been found, e.g., that XX females, X′X females and X′X′ females appear to be indistinguishable somatically except by the introduction of mutant characters, and that X(Y?) and X′(Y?) males are similarly indistinguishable. It has also been found that X′ carries the normal allelomorphs of the two mutant genes thus far identified in the X. On the other hand we have not succeeded in transferring either of the two genes mentioned to this chromosome—i.e., in combining them with the X′ differential. The latter point may have no significance, however, for the two genes exhibit less than 0.5 per cent crossing over in XX females. There is no evidence as yet to indicate whether the differential distinguishing X′ from X is a single gene or involves extensive differences between the two chromosomes, but it is clear that whatever the difference between them the two chromosomes are fundamentally similar.

THE CAUSE OF UNISEXUAL PROGENIES

If, as postulated above on the one scheme, the male transmits both X-bearing and Y-bearing sperms and the sex of the individual fly is determined by the type of sperm fertilizing the egg, it is evident that some selective process must operate to cause the progenies to be unisexual instead of typically bisexual.

Differential mortality might account for the observed results; but careful observations (Metz, 1929-b) have indicated that no such mortality occurs. The only other probable explanation would appear to be that of selective fertilization. On this hypothesis it is assumed that the eggs of female-producing females are fertilized almost exclusively by X-bearing sperms, the Y-bearing sperms being inactivated or eliminated, while in male-producing females the process is just reversed. It is impossible to actually observe such a process in this material, hence the hypothesis cannot be verified by direct observation. The indirect evidence, however, seems to be conclusive providing the assumption of two classes of sperms is correct.

On the other hypothesis, in which sex is determined by the type of chromosome elimination (during cleavage?) unisexual progenies would presumably be produced because the eggs of any one female would all (or practically all) go through the same process of development as regards this feature—either with or without elimination of the one sex chromosome from the soma. Here, as in the preceding case, the end result is determined in advance by the zygotic (sex chromosome) constitution of the mother.

DISCUSSION

Although the analysis of the problems here presented is far from complete, and many puzzling features remain to be cleared up, it may not be amiss at this time to present some tentative considerations on the general aspects of sex determination and sex ratios in *Sciara*. Numerous indications point toward the conclusion that the basic type of reproduction here is monogenic (giving unisexual progenies) and that the digenic type of behavior, found to occur characteristically in some species and more or less frequently in others, represents a modification of this

basic process. Since the monogenic type of behavior apparently depends upon selective fertilization or some other selective action taking place at or after the time of fertilization, it follows that anything interfering with this selection would tend toward the production of bisexual progenies. In the case mentioned above of the digenic strain derived from a monogenic laboratory stock of *S. coprophila*, females of male-producing constitution (XX) are modified so as to give varying numbers of daughters in addition to the expected males (unpublished data). Whether or not the digenic strains and species found in nature are genetically like this strain is not known, but the one found in *S. impatiens* (derived from a single wild female) appears to be of this same type. It would seem probable that various kinds of digenic strains might arise, differing according to the type of genetic changes which had occurred to produce them. On this basis it would be expected that in some cases a change or accumulation of changes would serve to eliminate the selective action entirely and produce strains or species giving typical 1:1 sex ratios. No such forms have yet been detected, but as suggested above this may be due to the presence of differential viability in some of the species studied. The question can be settled only by extensive experiments with digenic forms under carefully controlled and favorable conditions.

One of the most puzzling aspects of the general problem, if unisexual progenies are due to any such selective action as postulated above, is why this type of reproduction should be so widespread in the genus. It appears to be dependent upon a delicate balance which fortuitous changes (mutations) would be expected to break down, unless some distinct advantage inheres in the process. At present it seems necessary to assume such an advantage to account for the retention of the process in so many species, in spite of the fact that one of the most widespread and apparently successful species (*S. pauciseta*) appears to be consistently digenic in its mode of reproduction.

ADDENDUM

Since this paper went to press further studies on the chromosome group of the female germ-line have indicated that typically this group is like that of the male germ-line, and that the so-called "male-limited" chromosomes are not limited to one sex but to the germ-line of both sexes. (See Metz and Schmuck, Proc. Nat. Acad. Sci. 17: 272, May 1931.)

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FORMS OF NITROGEN ASSIMILATED BY PLANTS

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IN MUCH of the scientific literature, dealing with plant nutrition, the assumption is made that practically all the nitrogen which plants absorb from soil solutions is in the form of nitrates. It is generally known that ammonia and many organic compounds may be utilized also directly by plants, but the extent to which these are absorbed is usually considered to be very limited except under unusual conditions. It seems that this idea has become prevalent largely for the following reasons: (a) most of the nitrogen in soil solutions is in the nitrate form, and (b) nitrification is supposed to take place so rapidly that soluble nitrogen in forms other than nitrates can not, ordinarily, accumulate. A study of the available information on the subject would seem to indicate to the writer that a considerable portion of the nitrogen assimilated by higher plants, growing in *humid* regions, enters the root in forms other than nitrates. In this article a discussion is given of certain of the more recent investigations of particular interest in this connection.

In a practical consideration of the forms of nitrogen utilized by plants two questions must be considered: (a) what compounds can various plants use under ideal, controlled conditions, and (b) what compounds are available in soils for their use? The first of these questions has been discussed fully elsewhere and will be considered here only to such an extent as to furnish a background for the more interesting discussion of the second question.

FORMS OTHER THAN NITRATES USED UNDER CONTROLLED CONDITIONS

The ability of plants to assimilate many organic forms of nitrogen without nitrification has been repeatedly demonstrated. Hutchinson and Miller (10) have given an excellent review of the work done prior to 1911, as well as much original work, showing that a large number of organic compounds are utilized directly by higher plants. Brigham (3) found that, in general, organic compounds of high complexity are better after ammonification, while the simple compounds are not improved thereby. The work of Schreiner and Skinner (25) showing the utilization of many organic compounds, is also particularly thorough and convincing. The ability to utilize any given compound commonly varies widely with different crops and perhaps even with the same crop under different conditions. Certain investigators have also pointed out that while a given nitrogen source may not produce as good results as nitrate, yet if used in combination with other forms the final results may be better than nitrate alone.

The extent to which plants can utilize ammonia directly is of especial interest since it is the normal end product of the decomposition of practically all forms of nitrogenous organic matter. The earlier investigations, reviewed by Hutchinson and Miller (11), as well as their own work show that many agricultural plants grow normally when limited to ammonia

nitrogen, but that some plants seem to prefer nitrates. Pantanelli and Severini (16, 17) state that ammonia is more suitable for the formation of organic compounds than is nitrate. Best results were secured with those ammonium salts having anions that possess a nutritive value. Prianichnikov (19, 20, 21) and co-workers have also been leaders in this field of research and have stressed the necessity of adequate control of pH of culture solutions containing ammonium salts.

Jones and Shive (14, 15) secured better growths of wheat and soy-beans in nutrient solutions containing both ammonia and nitrates than in nitrate alone, provided the iron supply was adequately controlled. Prince, Jones and Shive (22) found that soy-bean plants, when given both ammonia and nitrates, preferred ammonia during the early period of growth and nitrate at a later date. Other work done at the same laboratory by Jones and Skinner (13) gave similar results. They showed further that ammonia nitrogen is readily absorbed from solution by the soy-bean plant even when the nitrate nitrogen content of the medium is several times as great as the ammonia nitrogen content. The absorption of ammonia nitrogen did not materially increase with increase in concentration of the ammonium salt in solution; on the other hand, where the nitrate concentration of the solution was increased the absorption of the nitrate by the plants did increase markedly.

Recently Pirschle (18) reported that plants usually gave as good growths on ammonia as on nitrates if the reaction was kept constant at pH6, while nitrates produced higher yields at pH 4.5 and 7.5.

An experiment by the writer, not previously reported, dealing with ammonia utilization by corn may be of interest here. The system recommended by Wilson (28) for growing plants under sterile conditions, was adopted with slight modifications. The seeds were sterilized by adding warm alcohol or acetone, mercuric chloride, and finally sterile water. The plants were grown in one liter bottles, containing a culture medium of the following composition, expressed as grams per liter: $CaCl_2$ — 0.45; KH_2PO_4 — 0.167; $MgSO_4$ — 0.167; KCl — 0.083; $FeCl_3$ — 0.001; and $CaCO_3$ — 1.0. To this medium was added 100 mgm. nitrogen per liter in the various forms. The dry weights of both the tops and roots of the corn plants are given in Table 1, the harvesting being done 90 days after germination when the tassels were just beginning to appear. In the case of calcium nitrate only one result is given due to breakage of the duplicate bottle.

In considering the results given in Table 1, it should be emphasized that in order to reduce the chances of contaminations the culture solutions were not changed or aerated during the growth period. The experiments were planned as a qualitative study of the response of the plants to nitrates and ammonia. It was realized that a strictly quantitative comparison would require the use of a larger number of plants, provision for periodic changing of the culture solutions, and the addition of the nitrogen at intervals.

The dry weights of the corn plants show that there is no reason to suppose that nitrate nitrogen is necessary for the normal growth of the corn plant, or that it is superior to ammonia nitrogen. This was true regardless of the fact that the ammonium sulfate was used at a concentration sufficiently high to cause a decidedly retarded growth for the first three weeks. At the end of the experiment there was no appreciable difference in appearance of the plants grown with

ammonium sulfate alone and those with the ammonium sulfate-sodium nitrate combination. The growth with sodium nitrate alone was rather disappointing due, probably, to the excess of sodium, which would affect the absorption of other ions. Calcium nitrate produced growth markedly superior to sodium nitrate but not equal to ammonium sulfate. Ammonium phosphate was not nearly as satisfactory a source of nitrogen as ammonium sulfate, but was slightly superior to sodium nitrate. The various forms of nitrogen used showed little difference in their effects on the time required to reach a certain stage of growth.

Tests for sterility, made on all solutions at the end of the experiment, showed that three of the bottles, designated in Table 1, contained a limited number of fungi. These contaminations were barely visible to the eye and apparently did not occur until about two weeks prior to the end of the experiment. Since fungi do not form nitrates, and since the infected cultures produced approximately the same growth of corn plants as the duplicates, it is not thought that the organisms appreciably affected the results.

Analyses for total nitrogen showed that the plants assimilated practically all of the nitrogen available regardless of the form in which it was supplied. The nitrogen content of the dry matter produced, therefore, varied inversely with the quantity produced.

TABLE 1

Dry weights of corn plants

TREATMENT	TOPS	AVERAGE	ROOTS	AVERAGE	TOTAL	AVERAGE
	gms.		*gms.*		*gms.*	
No nitrogen	1.02		.72		1.74	
	.87	.95	.65	.69	1.52	1.63
Ammonium sulfate	8.75		1.68		10.43	
	10.40	9.58	3.60	2.64	14.00	12.22
Sodium nitrate	6.25		1.80		8.05	
	6.36*	6.31	2.05	1.93	8.41	8.23
Ammonium sulfate 50% / Sodium nitrate 50%	9.16		2.99		12.15	
	10.22*	9.69	2.86	2.93	13.08	12.62
Calcium nitrate	8.30	8.30	3.46	3.46	11.76	11.76
Ammonium phosphate	7.19		2.13		9.32	
	6.45*	6.82	1.35	1.74	7.80	8.56

* Contaminated.

FORMS USED UNDER FIELD CONDITIONS

On the previous pages evidence is presented to show that most higher plants can assimilate ammonia and a large variety of organic forms of nitrogen in addition to nitrates. The main question is whether plants have available for their use any appreciable quantity of soluble nitrogen other than nitrates. Strictly quantitative information on the subject is necessarily meager because of the difficulties involved in such experimentation. There is a mass of information available, however, of an indirect nature that serves as a basis for judging what is taking place under field conditions. A few of the outstanding facts, particularly with regard to ammonia, are presented below.

Nitrates and Nitrites

Under average soil conditions most writers consider that nitrates are the chief, and in most cases almost the only, source of nitrogen for plants other than the legumes and a few unusual crops. Many studies have also been reported which apparently show that there is a correlation between crop growth and the nitrifying power of a soil. Such studies, as Gainey (8) has pointed out, often imply that fertility is more or less limited by the processes of nitrification. A careful analysis of the subject, however, led Gainey to conclude logically that "while nitrification is perhaps a valuable and even essential asset in fertility it probably does not, under normal conditions, become a limiting factor in productivity." He considers that fertility in normal agricultural soils in so far as nitrate nitrogen is concerned is limited by those processes necessarily preceding nitrification rather than by nitrification itself. Burd (5) also speaks of the tendency of students in soil biology "to regard determinations of the concentration or rate of formation of some specific end product of soil activities, such as nitrate, as conclusive of the effect upon soil fertility of the processes involved; whereas the author (Burd) has long believed that these latter have a more general significance." It is rather surprising that this view is not more generally held.

A thorough discussion of nitrate assimilation by plants seems unnecessary. No doubt nitrate nitrogen is the best source of nitrogen for the majority of plants and under conditions where nitrates are present in relatively high percentages, or where the conditions for rapid nitrification are favorable, it is safe to say that most of the nitrogen assimilated is in this form. Such ideal conditions, however, do not exist in the majority of soils, or even in the very best of soils throughout the year.

Nitrites may also be utilized by higher plants where the concentrations are low but they are so rapidly oxidized to nitrates that they ordinarily occur only in traces in soils and there is little reason for believing that plants secure much of their nitrogen in this form.

Organic nitrogen

Amino-acids and other simple water-soluble forms of organic nitrogen are intermediate products in the breaking up of proteins into ammonia. We know that ordinarily there is no accumulation of such compounds in soils because the microörganisms present use them for food. They either convert them into protein or break them up and discard ammonia as the end product. Higher plants do, no doubt, actively compete for the small quantities of soluble organic nitrogen but we know little about the quantities that they assimilate.

Ammonia

Ammonia, which is constantly being formed in soils, may or may not accumulate in appreciable quantities, depending upon conditions. In the discussion which follows, the subject will for convenience be considered under two headings—(a) special conditions, and (b) normal conditions.

Special conditions:—A few plants are known to thrive and produce normal growths where nitrification is practically impossible. Rice, for example, thrives on flooded lowland soils and responds better to applications of ammonium salts than to nitrates. Janssen and Metzger (12) state that it seems fairly well established that nitrate nitrogen does not perform a major rôle in the nutrition of rice

plants because (a) nitrates are reduced in a submerged soil and are nearly completely removed, and (b) the rice plant clearly prefers ammonia to nitrates as a nitrogen source. Many other plants are known to grow under similar conditions.

Hutchinson and Miller (11) make the following interesting comment regarding certain of the Rothamsted plots which 100 years ago contained an abundance of $CaCO_3$.

> It has recently been shown that the soil of some of the Rothamsted grass plots which have received ammonium salts for many years in succession has become distinctly acid and that, consequently, nitrifying organisms have become greatly reduced in numbers. Nitrification is limited to portions of soil directly in contact with the few particles of $CaCO_3$ still remaining in the soil. It is evident, therefore, that more or less of the nitrogen assimilated by the grasses must be in a form, or in forms, other than nitrate—probably mainly an ammonium salt.

Other information in substantiation of this idea has been supplied by Russell and Hutchinson (24). They showed that soils partially sterilized by heat or toluene produced larger crops of rye than did the untreated soils. They showed further that the treatment killed the nitrifying organisms but ammonia production was markedly stimulated. They attributed the increased productiveness of a partially sterilized soil to this increase in amount of ammonia present, which in turn resulted from bacterial action.

White (27) refers to the work of certain early investigators who found that forest soils do not contain nitrates, presumably because the acidity is too high for nitrification.

Albrecht (1, 2) made a study of soils under straw mulches and found that usually little nitrate accumulated because of excessive moisture and poor aeration. The ammonia content was higher in such soils, however, being as great as 22 p.p.m. in some cases. This is significant considering that many crops, particularly corn and potatoes, are known to grow unusually well under such conditions.

Stewart, Thomas, and Horner (26) made studies with pineapple plants from which they concluded that this crop is capable of assimilating all of its nitrogen in the form of ammonium salts. The authors were of the opinion that their data suggested that under field conditions the pineapple plant uses nitrogen in both the nitrate and ammoniacal forms.

It is common practice also to grow many crops on rather acid soils either because the crops prefer such soils or perhaps for the sake of controlling diseases. Potatoes, for example, are often fertilized with ammonium salts and the soil kept acid to control scab. Many other such special cases might be given where we are fairly certain that much of the nitrogen enters the plant in forms other than nitrates. It is not meant to imply, however, that no nitrification takes place in acid soils. Nitrates may be formed, as White (27), Fred and Graul (7), and many others have shown, but the process is greatly retarded.

Normal conditions:—Most soils contain comparatively small amounts of ammonia. Gainey (8) has summarized a considerable portion of the data reported prior to 1917. These results show variations from 0 to 69 p.p.m. with the majority of the figures between 5 and 20. In a few cases the percentage was higher than that of nitrates. Ammonia determinations made by Russell (23) on certain Rothamsted soils show that during the cold spring months ammonia may persist for several days or weeks following applications of ammonium salts or stable manure, but rapidly decreases when the soils become warm. Ordinary soils were found to contain about one or two parts per million, while rich soils contained 3 or 4. Using Russell's figures, an acre-foot of soil com-

monly contains 3 to 12 pounds of ammonia nitrogen; using American data these figures are considerably higher. The methods of ammonia analysis, used in the past, were not very accurate and allowance must be made for this fact in considering the data.

While quantitative data showing the ammonia content of soils are of interest the figures are likely to be misleading unless it is borne in mind that ammonia rarely accumulates to any extent; *it is constantly being formed and constantly being removed*. The total ammonia produced in an acre-foot of soil during a year might easily be as high as 200 pounds and yet an analysis might not show more than 2 to 5 p.p.m. at any given time. We know, however, that the soil tends to establish an equilibrium so as to maintain the ammonia content at a fairly constant minimum. A variety of agencies or factors are responsible for the disappearance of the ammonia, the chief of which are: (a) oxidation by nitrifying organisms, (b) utilization for growth by microörganisms, (c) assimilation by higher plants. A very slight loss may result from leaching and volatilization. Too often nitrification is about the only factor stressed.

It has frequently been claimed that nitrification is more rapid than ammonification, otherwise ammonia would accumulate in soils. This is probably true for most soils but only because the ammonifying organisms are limited to rather inert organic materials as food. If a considerable quantity of a material, such as dried blood, is added then ammonification may become 10 to 1000 times as rapid as nitrification. Very high percentages of ammonia (1500 p.p.m. or more) may accumulate with only traces of nitrates formed during short incubation periods (3 to 7 days). On the other hand, if we add ammonium salts to soils in optimum concentrations nitrate formation is relatively slow. Ammonification is, therefore, inherently a far more rapid process than nitrification. The chief reason for the differences in rates is that two types of compounds and two groups of organisms are involved. The foods used by the ammonifiers may be considered as essentially combinations of carbohydrates and ammonia. They attack these compounds (proteins, amino-acids, etc.) primarily in order to get the energy of the carbohydrate and incidentally liberate the ammonia. On the other hand, the nitrifiers attack the ammonia in order to obtain energy by oxidation of the ammonia, itself, rather than associated materials. In both cases energy is the chief thing desired by the organisms and it merely happens to be the case that under ideal conditions one energy-producing process is much more rapid than the other.

The disappearance of ammonia from soils as a result of the growth of soil microörganisms, other than the nitrifiers, is due to the fact that these organisms require available nitrogen for the construction of their own body protein. Most of these grow just as well, or even better, with ammonia as with nitrates. The quantity used by these organisms varies widely with the numbers present, temperature, food supply, etc. If organic matter that has a very high carbon-nitrogen ratio is being rapidly decomposed, very frequently almost all traces of all forms of soluble nitrogen are used; if the ratio is low, then the decomposition processes commonly result in the liberation of more ammonia than is needed by the organisms themselves.

Our knowledge of the quantity of ammonia assimilated by higher plants growing in field soils is very limited. Analyses of soils for ammonia might indicate that it is of little importance, but the

fact that it rarely accumulates does not justify such a conclusion. Even the nitrogen assimilated by higher plants as nitrate must first pass through the ammonia stage, where both higher and lower plants compete for it. We know that both groups of organisms can remove practically the last traces from the soil solution. We know, furthermore, from the work of Prianichnikov (21), Shive and his co-workers and many others that ammonia is absorbed by plants at a very rapid rate—more rapidly than nitrifying bacteria can oxidize it. To these facts we should add the very important findings of Jones and Skinner (13), previously mentioned, that certain plants decidedly prefer ammonia during the early stages of their growth. Burd (4) has shown that in the case of a crop such as barley most of the nitrogen required by the plant for its entire growth is assimilated during the period of 6 or 7 weeks beginning when the plant is 3 weeks old. Assuming a normal nitrogen supply the quantity absorbed is roughly proportional to the green weight of the plant during this growth period; with an excess of nitrogen the young plant will store it up to a considerable extent.

Nitrification ordinarily proceeds rather slowly in humid regions during the spring months when crops require the most nitrogen. This is particularly true in the North, where the temperature effect is intensified by the fact that most of the soils are rather heavy; hence they retain more water and for longer periods following rains than do the soils of the South, which are largely sandy. Even the total supply of all forms of available soil nitrogen is usually not sufficient for the optimum growth of plants in the early spring. Burd (4), Burd and Martin (6) and Hoagland (9) have stressed this point. This fact is so well known and so general that the use of nitrogenous fertilizers for speeding up the growth of early crops, especially leafy vegetable crops, is almost universal. Even in the South the same practice is recommended for cotton in order to hasten plant development and lessen boll weevil injury. Too low a temperature, high acidity, poor aeration, or excess of organic matter may greatly retard nitrification. In addition, where the rainfall is heavy, denitrification may be a considerable factor. Under such unfavorable conditions ammonification may be retarded also but to a less extent than nitrification. If both processes are slow, higher plants can still use ammonia supplied as a fertilizer. Many soils which might nitrify sufficiently rapidly to produce enough nitrate to supply the plant needs if given the entire season, certainly can not fully meet those needs if given only a period of about two months during the spring season to do it. Is it likely that plants growing in soils deficient in nitrates fail to assimilate ammonia (constantly being formed or added in fertilizer) and other protein decomposition products, particularly when practically all of these are excellent plant foods?

In closing, it is well to state that while emphasis has been placed on the direct absorption of forms of nitrogen other than nitrates, it is not to be assumed that nitrates are of minor importance. So much emphasis has always been placed on nitrates that there is no need for further facts along this line. The writer has merely taken for granted that under average field conditions nitrate nitrogen is probably the most important nitrogen source for crops, but has pointed out that other forms may also be utilized to a greater extent than has generally been supposed.

SUMMARY

1. A brief review is given of previous investigations dealing with the forms in which nitrogen can be utilized by plants. In addition to nitrates it is shown that many organic forms of nitrogen and ammonia are assimilated by higher plants. Many recent investigators have found that ammonia is usually as satisfactory a direct source of nitrogen for plants as nitrate, provided the H ion concentration is kept low; while some plants, especially when young, decidedly prefer ammonia.

2. A report of an experiment with corn, grown in solution cultures with various ammonium salts in comparison with nitrates, showed that under the conditions there was nothing to indicate that nitrate nitrogen was necessary for the normal growth of corn or was superior to ammonia nitrogen.

3. A discussion of ammonia utilization by plants grown in field soils is given. It is pointed out that there is very little information on this point, but the available facts seem to indicate that a greater percentage of the nitrogen assimilated by higher plants under field conditions may be taken up in forms other than nitrates than is generally supposed. This is particularly true in the humid regions where the majority of the soils are acid, where the rainfall is heavy in the spring, and where the soil warms up rather slowly.

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THE VACUUM TUBE OSCILLATOR IN BIOLOGY

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WE ARE already familiar with the far reaching effects obtained in biology by the use of gamma rays, of x-radiation, of ultra-violet, of light and of infra-red. We know that all of these form one great, continuous spectrum of electromagnetic waves, the various regions of which differ only in wave-length. Beyond the near infra-red, as we know, is the radiation used by radio, which extends this spectrum into regions of very long waves, now commonly called Hertzian or electric waves.

Although this spectral band is continuous there are still gaps not yet adequately filled by instrumental means, as, for example, the gap between x-rays and ultra-violet. Another great gap, now being rapidly filled, lies between the near infra-red and the waves of wireless. It is only recently that short wave radio transmission became possible and this advance has led to a continued reduction in the length of waves obtainable. This has largely been made possible by improvement of the three electrode vacuum tube.

The invention of this tube has been the door which opened to the biologist a whole new world of radiation. The region is inconceivably vast, extending, as we know, from the near infra-red to a theoretical infinity, and it might seem quite difficult for him to decide upon some locality as most suitable and promising for experimentation were it not for certain practical and mechanical restrictions. The limitations of the vacuum tube make it very difficult to obtain wave-lengths of much less than a meter, so that the region of shortest electric waves cannot at present be explored. Again, apparatus generating wave-lengths much longer than 100 meters is not convenient in biology; and the experimenter has for the time being confined his research to a range of wave-lengths of from 1 to about 100 meters.

It is here, then, in the region of relatively short electric waves that we find the biologist utilizing the modern development of the vacuum tube and associated oscillating circuits. He is using equipment ready at hand, easily obtained and at much lower cost than almost any other physical apparatus. Properties inherent in the vacuum tube permit him to select a definite wave-length and to maintain that wave-length in relatively pure form throughout the duration of his experiment. In this way he may probe with some confidence the properties of various wave-lengths within the range of his apparatus. This is not the case in the usual type of high frequency apparatus used for therapeutic purposes—diathermy. Here, the oscillations are produced by condenser discharge through a spark gap. The oscillations produced in this way are a composite of many waves of various lengths, and consistent operation at the wave-lengths worked with in the experiments here reported is impossible.

The biological effects of high frequency oscillations generated by the vacuum tube

appear to have been first investigated by Gosset and his co-workers only six years ago, but since that time much of great promise has been accomplished by biologists in widely separate fields of research —the production of artificial fevers; the attenuation of diphtheria toxin; the treatment of malignant tumors; the acceleration of plant growth; the study of nervous reactions, of respiration and of tissue regeneration.

Gosset, Gutmann, Lakhovsky and Magrou, 1924, studied the effects of very high frequency radiation upon plant tumors caused in the geranium by *Bacterium tumefaciens*. They reported that three geranium plants bearing tumors caused by inoculation with the bacterium were exposed to radiations emitted at a frequency of 150,000,000 cycles per second. The plants were given various exposures on consecutive days and after 16 days from the first exposure the tumors, after growing in the interval, began suddenly to necrose. The necrotic process was said to be complete in about 31 days, so that the tumor could be detached by slight traction. In 16 control plants the tumors grew rapidly to enormous size and recurred after surgical excision.

Schereschewsky, 1926, seems to have been the first to subject animals to the action of high frequency oscillations generated by the vacuum tube. He placed small laboratory animals (mice) in a box of insulating material held in the field of a condenser resonating a tuned circuit. He found that exposure caused severe symptoms which might result in death if the exposure was prolonged more than a few minutes. Part, at least, of these symptoms he thought to be due to heat retention. Besides this acute lethal effect, exposure, he found, caused destruction of tissue. After sublethal exposures, in many instances, small hemorrhagic areas were observed along the course of blood vessels of the ears and within a few days the ears became necrotic and dropped off. This was also true of the tail. He believed that his experiments indicated a differential action with respect to frequency and that frequencies of highest lethality lay between 18,000,000 and 66,000,000 cycles per second. Finally, he remarked that here was a band in the spectrum of radiant energy which as yet had been little studied in its effects on living cells.

In his first paper, 1926, Schereschewsky described in detail the construction of his apparatus. For the more important of his experiments he used the type of oscillator originated by Huxford, 1925. Christie and Loomis, 1929, continued these descriptions of suitable circuits for biological experimentation and McKinley, 1930, described a convenient apparatus for treatment of small laboratory animals and materials. Unlike most physical apparatus the high frequency generator is surprisingly easy to assemble, and this in itself gives promise of its wide application in biology.

In all of these circuits the experimental animal, insulated in a box of nonconducting material, is placed in the field between the plates of a condenser which is part of a circuit excited by the oscillator at some particular frequency. Consequently, as pointed out by Schereschewksy, no free electrons from the external metallic parts of the circuit can enter, nor can they flow out from the body of the experimental animal. The animal, however, is subjected to a displacement current, in which electrons in the molecules of the body cells will, according to their state of freedom, either pass from molecule to molecule, first in one and then the other direction, or, if bound, are stressed in a direction the polarity of which alternates at the oscillator frequency.

THE TREATMENT OF MALIGNANT TUMORS

Schereschewsky believed that frequency was an important factor in the action of these oscillations and the thought occurred that, under suitable conditions, oscillations at certain frequencies might prove more injurious to some tissue cells than to others. To test this he chose the tissue cells of transplantable tumors because here he had groups of cells distinctly different from adjacent body cells, not only in size but in rate of proliferation. He selected for his experiments a most virulent mouse sarcoma, implantation with which yielded 95 to 96 per cent of takes. Treatment was localized as far as was possible to the cancer cells, the tumor being placed between small insulated plates. Frequencies from 60,000,000 to 150,000,000 cycles per second were used.

Soon after beginning his experiments he noted that in favorable cases treatment had a pronounced effect upon the tumor, the mass seeming to become much smaller and softer almost immediately after exposure. In these favorable cases the tumor and affected area around it came away within 10 days to 2 weeks, leaving the skin pink and healthy beneath it. Many technical difficulties arose during the course of these experiments but the most troublesome was the association of this tumor with a diphtheroid bacillus, which of itself is pathogenic for mice. Many mice were lost from this cause even after the tumor had apparently receded completely. However, despite all difficulties, of 403 mice which he treated 100 recovered tumor free. No case of spontaneous recession of the tumor was observed in 230 control mice, all of which died in from four to six weeks from the date of implantation. Schereschewsky and Andervont, 1928, performed similar experiments upon a transplantable fowl sarcoma. The tumors were implanted in the skin and combs of adult chickens, several of the birds being used many times after having recovered from successive implantations. In these experiments 61 per cent of the tumors receded completely.

So much for the brighter side of this picture. Christie and Loomis, 1929, in a very careful study of the effects of high frequencies on mouse sarcoma were unable to duplicate the promising results of Schereschewsky. Their experiments led them to believe that treatment in the high frequency field was not only ineffective in controlling tumor growth but that there was no evidence to support the contention that there is a differential action upon tissue cells with respect to frequency. They were impressed with the fact that the lethal effects of exposure in the high frequency field seemed to be due entirely to retention of heat to a degree incompatible with life. Kahler, Chalkley and Voegtlin, 1929, were also impressed with this heating effect and came to the conclusion that the only demonstrable effect, as far as their material was concerned, was primarily caused by a temperature increase in the organism. They worked with a protozoan (*Paramoecium caudatum*).

IS THERE A SPECIFIC ACTION APART FROM HEAT PRODUCTION?

The ultimate value of the high frequency field in cancer research is, then, an open question, as is its possible differential action on various tissues of the body. At the moment investigators in the field seem to be more concerned with the observed heating effects, a matter of undoubted importance, for, if the effect is purely one of heat, it might seem rather useless to obtain it in this way. The generation of heat is probably due, as has been pointed out, to severe displacement currents set up in the body of the animal by the action

of the field. The heat is, of course, internal and has been used, as will be seen later, to obtain any degree of synthetic fever. Consideration of the high frequency field from a purely physical point of view might lead one to expect, a priori, that it would be possible, providing one used the proper material, to demonstrate a secondary effect independent of the heat factor. This, it seems, is just what at least one experimenter has shown.

Szymanowski and Hicks, 1930, working at 158,000,000 cycles per second have been able to definitely attenuate diphtheria toxin without elevating the temperature to a level which would by itself affect the toxin. The control in this experiment was very carefully worked out and the results so uniform as to leave little doubt that there is a specific action of short electric waves other than the heat produced by conductivity and eddy currents. These two experimenters are now interested in the action of the high frequency field on the two other major toxins, botulinus and tetanus, and in the suggestion of D'Arsonval that the irradiated diphtheria toxin should be investigated with regard to its properties as an immunizing substance. McKinley, 1930, also obtained certain results indicating a specific action. Exposure of the whole of the vertebral column of the frog at 90,000,000 cycles per second resulted in all cases in an immediate and strong response, the effect, a violent muscular contraction, being observed in the hind legs. These experiments were repeated with external heat as the agent and the characteristic reaction of leg muscles as observed for high frequency dosage failed to take place.

Besides these experiments in which the vacuum tube was the physical means there are at least two investigations in diathermy which point to effects other than heat—those of D'Arsonval, 1914, and Bennedetti, 1926. D'Arsonval worked with irradiated toxin in experiments similar to those of Szymanowski. Bennedetti treated the seeds of several varieties of common garden plants. He used a Rumkorff coil and spark excitation, making his exposures in a combined electromagnetic and electrostatic field. Treated seeds, he found, germinated and grew more rapidly than controls. Treatment raised the temperature of the seeds about ½ degree centigrade, and, in order to compensate for this factor, he kept all controls at the temperature of the radiated seeds for the duration of the exposure. His results led him to conclude that the small temperature rise due to the field of exposure was not the cause of the favorable germination and growth-rate in treated seeds. McKinley, 1930, using the vacuum tube oscillator treated the seeds of Golden Bantam corn and obtained a slight acceleration in the early germination period, but these experiments have not yet been correlated with the heat factor.

THE PRODUCTION OF SYNTHETIC FEVERS

Carpenter and Page, 1930, taking advantage of the very quick and certain heating effect of exposure to the high frequency field were able to obtain synthetic fevers in animals, including man, without the injection of foreign substances. They followed the suggestion of Hosmer, 1928, who had studied heating effects on salt solutions of various concentrations and on small laboratory animals, and have contributed a therapeutic agent of very great possibilities. By proceeding cautiously they were able to treat 25 human patients, obtaining fevers of 104 to 105 degrees fahrenheit in 60 to 80 minutes. The patient was suspended in the field so that the waves oscillated through the body from one side to the other; the head was not exposed. They were careful to use

the lowest possible current and seem to have avoided entirely all the skin and muscle blistering found by Hosmer and by MacCreight and McKinley, 1930, to accompany hard dosage. All of their patients showed no ill effects, complaining only of slight nausea or headache during exposure.

Carpenter is convinced that in spite of the crudities of the present day apparatus this method of obtaining artificial fevers is not only practical but efficient and will prove of great value to the clinician, physiologist, biochemist and bacteriologist. He also studied the relation of this synthetic fever to infectious diseases in laboratory animals and believes that two desirable effects are obtained by raising the body temperature. First, the increased heat within the body makes a less favorable environment for the multiplication of virus. Second, the heat increases the rate of those chemical processes concerned with the development of immunity and with the general defense mechanism of the body against infectious agents.

The investigation of artificial fevers has been taken up by several medical centers in the United States and Canada, but especially at the University of Rochester under the direction of Carpenter, J. R. Murlin and S. L. Warren. Unpublished results indicate that high frequency oscillations may be an effective agent in the control of such diseases as paresis, gonococcal arthritis and syphilis. Experimentation along this line has been carried on with human patients, and the preponderance of favorable results has encouraged the investigators to continue.

Schliephake, 1928, '29, investigated lethal effects on mice and various insects in connection with a nervous hypersensitivity, finding that brain tissue has the highest heating rate, and he, with others, believes that high frequencies are more or less specific for nervous tissue. Headlee and Burdette, 1929, found for insects that the nervous reaction speeds up the rate of producing internal heat; the more specialized the nervous tissue the greater the increase in speed of reaction. Of many organic chemical compounds which they measured they found that cholesterol, which is characteristic of nervous tissue, had the most rapid heating rate. McKinley, treating holometabolous insects, where there is a marked difference between the nervous organization of the larva and the adult, found that the lethal time of the larva was about six times that of the adult. In hemimetabolous forms, where there is little difference in the nervous organization of the nymph and adult, the lethal time was about the same.

Schliephake made careful studies of comparisons of heating rates in diathermy and the modern high frequency oscillator. He found that in diathermy the greater heating effect is in fatty tissues. In the high frequency condenser field the heating was found to be more evenly distributed in all the tissues. His experiments showed that the modern condenser field as compared to diathermy has a much greater depth of action.

Exact comparisons between the condenser field and diathermy, or comparisons of the effects of various frequencies, are very difficult at the present moment. For this reason development of methods to measure accurately the output between the exposure plates is eagerly awaited. Until he has this measurement the investigator has little more than an opinion to offer when he speaks of the differential action of various wave-lengths. Schereschewsky believes they are distinctly selective; Christie and Loomis doubt the possibility. Schliephake was led by his experiments to conclude that a change in wave-length brings about a change

in rate of heating of various tissues. Baldwin and Nelson, 1929, however, after work on histological preparations of tissue from rats killed by high frequencies concluded that there was no selective action.

It is perhaps probable, as pointed out by Schereschewsky, that the wave-lengths now being used are too far removed from any possible natural period of body cells or cell aggregates. This natural tissue wave-length, which he estimates to lie between 0.5 and 3 or 4 millimeters, is, as has been stated, beyond the possibilities of the present day vacuum tube. Such a wave-length lies very close to the near infra-red and the lowest wave-length yet secured with the vacuum tube is about 40 centimeters. We might say, then, that the utility of the three electrode vacuum tube in biology has already been well established, but that it is, nevertheless, still a rather crude instrument. Much of this crudeness will no doubt be corrected within the next few years; and it may even be that the physicists will give us a tube with which we may reach these hypothetical tissue frequencies—with which we may perhaps, treat some one body organ without in any way affecting the others.

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THE PROBLEM OF COLOR VISION IN FISHES

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THE PREFERENCE METHOD

EVIDENCE on color vision in fishes is conflicting. Because of the fact that certain fishes rather consistently respond either positively or negatively to light, it has seemed convenient to certain experimenters to use the preference method in the investigation of color vision in these animals. If it could be shown that a fish, repeatedly forced to choose between two lights differing in wave-length only, always or nearly always selected the same one of these lights (position and other variables being controlled), it would seem impossible to deny that the animal was capable of differential response to wave-length. It should be said at once that no investigator has presented conclusive evidence for such behavior. None has satisfactorily controlled the intensity factor. Even Hess, who has taken more pains than have many others, failed at this point.

Graber (19) was perhaps the earliest investigator to use the preference method in an attack on this problem. He found with the fresh water fishes, *Cobitus barbatula* and *Alburnus spectabilis*, a preference for the dark rather than the light, for blue without ultraviolet rather than blue with ultraviolet, for red rather than green and for green rather than blue with ultraviolet. The following year (20) he obtained about the same results on the marine forms *Gasterosteus spinchia* L. and *Syngnathus acus* L. Furthermore he found that it was possible to reverse the preference for red over blue by using an intensity of the former twenty times as great as that of the latter. Although Graber's work appears to indicate wave-length discrimination it cannot be accepted as anything more than a suggestion because of technical flaws. The colors were produced by pigmented glass and the intensities were "equated" by using pairs of colors which appeared to be equally bright to the human eye. The source of illumination is not given. Graber described the distribution of the fishes thirty minutes after the beginning of the light stimulation conditions. Hess (25) criticizes him for not also reporting the immediate responses.

The work of Bauer

Bauer (2), using the preference method, came to the conclusion that fish and man differed but little with respect to color vision. The apparatus used was a narrow "phototaxis basin" painted black on all sides but one. This basin, containing the fishes, was placed within a black box, one side of which (that corresponding to the clear glass side of the basin) contained openings into which two filters could be fastened, each extending over one half of that side. The filters were of gelatine, paper or glass and the wave length for each was noted. On the side opposite the filters was a hole for the use of the observer. The light intensity was regulated by moving the source of the light (not described) back and forth. To avoid heat from the light an intervening "water box"

was employed. Bauer also used spectral lights in a part of his work. *Charax puntazzo* Gm., *Atherina hepsetus* L., and *Mugil sp.* were used. If unfiltered light (white?) was thrown into one half of the basin, the other half being dark, neither positive nor negative phototaxis was shown. The fishes swam back and forth into and out of the lighted part of the basin. A positive response was given, however, to change of almost any kind. If a piece of white paper were placed at the open side they assembled at that point. They again assembled when the paper was removed or replaced by another. However, if the intensity of the light was made very strong the fishes rushed to the darker part of the basin. The above behavior was found in both photopic and scotopic animals. When photopic fishes were tested with colored lights, using an intensity too low to arouse negative responses, strongly positive movements were observed in the case of blue, green and light yellow. Red light called forth immediate and violent negative reactions. When spectral lights were used, starting from the violet end of the spectrum and gradually increasing the wave-length, this negative reaction was first definitely observed at 610 mμ. In the tests described but one part of the basin was illuminated at a time, the other half being dark. If the two halves of the basin were illuminated by different colors, one of which was red, the fishes in the red half gave pronounced negative reactions to the source of light until they happened to get into the other half when they at once reacted positively. Once in this light they never returned to the red. Bauer did not control the intensity factor directly but maintained that this differential behavior was not due to intensity differences since, when the two halves of the basin were illuminated by white light of different intensities, the animals swam back and forth from one to the other, indifferently.

Further evidence of color vision is offered by Bauer using *Box salpa* L. This species is positively phototactic to a marked degree. When a piece of frosted glass was placed in the filter frame and then, in addition, a piece of blue glass placed over one half of the frosted glass, the fishes assembled in the blue half. Since, Bauer says, the blue half must be darker than the other half, the response is contrary to the normal positive phototaxis and must therefore be determined by color rather than by intensity.

Bauer's general conclusion is that photopic fishes can distinguish differences in wave-length; that scotopic fishes may or may not be able to make such a discrimination.

The work of Hess

Hess has so frequently reported studies using the preference method that detailed consideration cannot be given each. In his best application of the method the light from a Nernst globe was passed through a prism and the resultant spectrum thrown against the side of an aquarium. All other light was excluded. Within the aquarium were usually a large number of young fishes, as many as sixty in some cases. The distribution of these fishes in terms of the percentage which congregated in the various parts of the spectrum was noted. It seems that it would have been better to have used a longer and narrower tank than that used by Hess (27 by 18 cm.) in order to keep more uniform the extent to which the light was transmitted through the water before reaching the various fishes. A wide variety of fishes, both marine and fresh water, were studied. It should be noted that Hess does not report results for all of the species used since some of them (young brook trout, eels, pike and "*Saiblingen*") did not give "sufficiently useful results." Just what determined whether

a result was useful or not is unknown. Hess used young fishes almost entirely, doubtless because their behavior was more uniform. For this he has been criticized by Reeves (39), a criticism based on Shafer's work (46) which seems to indicate that the retinal cones of young fishes and of older fishes are quite different.

Hess reports that the majority of the fishes gather in that part of the spectrum

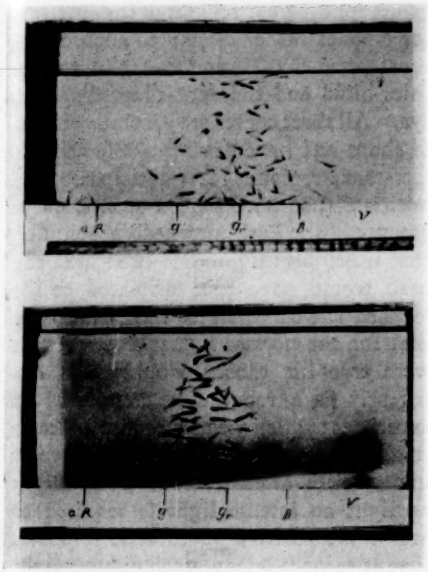

FIG. 1. TWO PHOTOGRAPHS FROM HESS SHOWING CONCENTRATION OF YOUNG FISHES IN THE YELLOW-GREEN PORTION OF A SPECTRUM

bounded by the Fraunhofer lines E and b (that is wave-lengths of 525 to 535 mμ) (Fig. 1). Light of this wave-length would be described by man as green to yellow-green. Since with various intensities of white light these fishes always responded positively to the brightest, it might be said that for them this region of the spectrum appeared the brightest. Not all of the fishes remained in this part of the spectrum. Toward the red end they thinned out rapidly; toward the violet end, not so rapidly. It has been said above that Hess did not control the intensity factor. He appeared not to recognize the fact that a prism does not transmit, with the same amount of loss, light of different wave-lengths. Prisms of different materials vary in the relative efficiency with which they transmit light of various wave-lengths. Unless the characteristic of the prism used is known, and this factor compensated for in some way, different parts of the spectrum thrown by it from a single source of light cannot be known or expected to possess the same intensities. Were we to waive this criticism and accept Hess's assumption that all parts of the spectrum were of uniform intensity we would suppose at first sight that his data indicated color discrimination. To Hess, however, just the opposite is indicated. To him the uneven distribution of the fishes does not represent color preference. Rather, it shows that the brightness value of equally intense lights of different wave-lengths is not the same. A yellow light, for example, has a greater stimulation value than a blue of equal intensity. We assume, perhaps, that each is seen as a gray, but that these grays differ in shade.

In further experiments fishes were tested in a tank lighted not by a spectral band but by two lights, a control light from a Nernst lamp and a monochromatic light obtained by using a very restricted part of the spectrum. The control light was so arranged that its intensity could be varied by the adjustment of its distance from the tank. By keeping the prism and its source of light at a constant distance from the tank Hess expected to be able to produce monochromatic lights of any wave-length desired but always of the same intensity. (But see criticism above.) Starting with the spectral green (lines E to b) lighting one half of the tank he so

adjusted the intensity of the control light thrown into the other half that the fishes distributed themselves uniformly throughout the tank. Under these conditions he presumed that the brightness value of the control light was equal to that of the spectral green. The distance separating the control light from the tank was then taken as unity. The spectral rays were so shifted that first one and than another section took the place of the E-b portion. For each color the control lamp was readjusted, nearer or farther from the tank, until a uniform distribution of the fishes

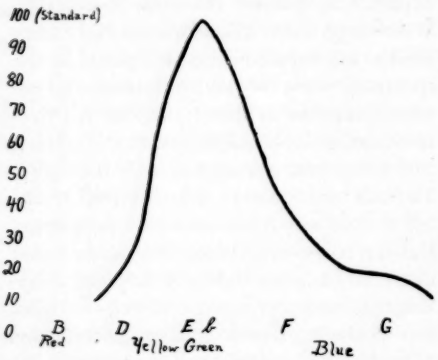

FIG. 2. THIS CURVE, BASED UPON DATA FROM HESS ON YOUNG FISHES, INDICATES THE BRIGHTNESS VALUES FOR LIGHT OF DIFFERENT WAVE-LENGTHS

was again obtained. The distance in each case was noted and expressed in terms of its relation to the distance necessary to obtain uniform distribution for the spectral green. The accompanying graph (Fig. 2) constructed from his data indicates the character of the results. It will be noted that the green or yellowish green portion of the spectrum has the highest brightness value. As the wave-length is increased from this point the value falls off rapidly, becoming zero in the red end of the spectrum. As the wave-length is decreased from this high point the reduction in brightness value is more gradual.

Verification of a sort is to be found in another of Hess's experiments in which each of the two halves of the tank was lighted by a monochromatic light of (supposedly) the same intensity. In general the fishes gathered in that color which, as measured by the method described above, possessed the highest brightness value.

The point which Hess emphasizes continually is that this curve of brightness-values for different regions of the spectrum corresponds rather closely to such curves constructed by Hering for the totally color-blind and the dark-adapted human eye. All three curves are generally similar in shape and have their peaks in the yellow-green region. Hess anticipated the criticism that he obtained such a curve because of the Purkinje phenomenon; i.e., that if brighter lights had been used the peak would have been displaced to the left and the curve might have resembled that for the normal human eye. If this were true his theory would fall. Apparently as a rebuttal he performed an experiment which seems to indicate clearly that when fishes are tested in a dark room immediately after removal from bright daylight an intense light is required to arouse the positive phototactic response; that 45 seconds later a much dimmer light will suffice; that 15–20 minutes later a light having but 1/1000 the intensity of the original light will arouse the response. It is difficult to see why he considered the demonstration of the similarity of the fish and the human eye with respect to darkness adaptation a reply to the criticism that his results would hold only for the degree of brightness he used. His only "proof" lies in the statement that "I could show that within a wide range of absolute light intensities the sensibility of my fishes for differences in brightness is obviously similar to or the same as ours, so

that the higher light intensities—for us—can not have a relatively lesser stimulation value for the fish, which disproves the aforementioned possibility [that the curve obtained holds for only a limited intensity range]."

More recently (30) Hess has reported further experiments relating to these problems but in general they do not differ essentially from his earlier work either in their execution or in the conclusions drawn from them.

A further similarity between response to color in fishes and in the totally color-blind human claimed by Hess is that in

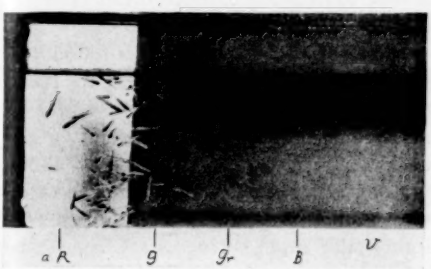

FIG. 3. PHOTOGRAPH FROM HESS SHOWING YOUNG WHITEFISH BEING DRIVEN TOWARD THE RED BY THE GRADUAL CUTTING OFF OF THE SPECTRAL LIGHT BEGINNING AT THE VIOLET END

both cases there is a shortening of the red end of the spectrum. He states that a fish simply fails to respond in any way to light of this quality. In one case in which the tank was illuminated by the entire visible spectrum he commenced cutting off the light, beginning at the violet end. The animals, being positively phototropic, left the darkened part finally being all driven up to the orange portion, all shorter wave-lengths having been eliminated (Fig. 3). As the process was continued they even congregated in longer wave-lengths (620 to 640 mμ) but when only wave-lengths of 650 and over remained the animals distributed themselves evenly throughout the aquarium just as they would if all light were cut off. Bauer (2), however, failed to verify these results. He found that photopic fishes gathered in darkness in preference to red light (680-710 mμ) and that scotopic fishes gathered in the red light in preference to darkness.

One of Hess's experiments (25) upon the sensitivity of the fish-eye to red is so simple in its execution that it is surprising others have not attempted to verify it. In a dark room the aquarium was illuminated by a Nernst lamp in front of which a red glass was held. A wriggling worm was then thrown into the basin. The fishes paid no attention to this food even though the worm was clearly visible to the experimenter. When the red glass was replaced by a blue one, appearing much darker to the human eye, the worm was at once seized and eaten. Incidentally this experiment indicates that for the species used (not mentioned) visual stimulation was more important than olfactory in the food-seeking behavior of the animals.

Using *Mugil sp.*, a positively phototactic form, Bauer offers evidence that the Purkinje phenomenon occurs in fishes. Photopic animals were given the choice of green or blue, the intensities being so adjusted that the fishes assembled in the green half. Reduction of the intensity (supposedly equivalent for the two colors) reversed the preference, the fishes then gathering in the blue half. Hess criticized Bauer for using green and blue for testing the animals for the Purkinje phenomenon, saying he should have used the customary red and blue. Bauer's reply was that he could not use red because of the "red-fear" which he had found in photopic fishes.

Hess claims that the differential behavior of photopic and scotopic fishes is quite unlike the Purkinje phenomenon and that the latter cannot be demonstrated. He holds that in light-adaptation there is a

pigment, interspersed between the rods and cones and having the power to absorb the shorter wave-lengths. This so arranges itself that it intercepts and absorbs a large part of these wave-lengths before they strike the retinal elements. During dark-adaptation this pigment recedes in such a way as to be much less effective. If, then, the intensities of two lights, one red and one blue, were so adjusted that for the dark-adapted fish (positively phototactic) an indifferent distribution in both halves of the basin were attained, then light-adapted fishes would gather almost exclusively in the red half (since in such fishes the pigment would reduce the efficacy of the blue). In one rather neat experiment which seems to demonstrate clearly the distinction between the Purkinje phenomenon and the effect of dark and light adaptation, dark-adapted fishes were given the choice of red and blue, both lights being of very low intensity. To the experimenter's eye both surfaces appeared almost colorless, the blue being much brighter than the red. The fishes gathered in the blue half. Then, by removing a shutter and moving the sources of light nearer, the intensity of the two colors was greatly increased. To the experimenter's eye (being subject to the Purkinje phenomenon) the red now appeared much brighter. But the fishes still remained in the blue part. Hess states that the characteristics of dark-adaptation persist for a minute or so. After that, supposedly, light adaptation sets in, the pigment becomes effective in reducing the efficacy of the blue and the fishes may approach the red. In a further experiment the blue and red were equalized for dark-adapted fishes at an extremely low intensity. No increase of intensity (equal for both colors) could disturb the uniform distribution of the fishes. Hess's point is, then, that the Purkinje effect is observed immediately upon the change in intensity of the spectral colors and before the elapse of the minute or more required for adaptation. This immediate shift in the relative brightness values does not occur in fishes. What has been mistaken for this phenomenon (the relative reduction of the efficacy of the shorter wave-lengths with increased illumination) is not the result of the increased intensity of the spectral colors, as such. Rather it is the result of the pigment migration accompanying or constituting the adaptation to any change in general illumination. The fact that this adaptation requires an appreciable lapse of time enables one to differentiate between the two phenomena.

For light-adapted fishes Hess found the yellow-green to green portion of the spectrum to be the brightest. The degree of intensity necessary to equate any other color with pure yellow was only about half of that necessary to equate that color with yellowish green. With the spectral lights, the intensity necessary to equate pure blue with a constant yellowish red was four times as great for light-adapted as for dark-adapted fishes.

It is to be expected that the results reported by Bauer (and others) and by Hess would not be in agreement even though all made use of the preference method. Several possible explanations for the conflicting results are obvious. Only two of these will be mentioned, and these largely because they are in themselves problems of considerable theoretical importance. First, the best evidence for color discrimination that Bauer offered, was in the case of photopic fishes. Most of Hess's observations, on the other hand, seem to have been on scotopic animals although it is true that he makes general remarks to the effect that photopic animals react similarly. Bauer holds that under the two extremes of adaptation fishes react quite differently,

especially to the longer wave-lengths. Secondly, both Hess and his opponents assume that a phototaxis furnishes a form of motivation which can be relied upon to be consistent in strength and direction from individual to individual within a given species, and from one time to another for an individual. Perhaps the reconciliation of the conflicting results which have been reported is to be found not in flaws of technique (though these exist in abundance) but in the assumption that these taxes are flexible and that there are many factors, internal and external, which may alter their degree and even their direction.

A brief summary of Hess's work will be given at this point although other of his studies must be mentioned in later sections. First will be listed criticisms which may be advanced against his studies:

1. He does not seem to recognize the possibility that response to intensity, even though it may dominate response to color, does not necessarily exclude the possibility of the latter.

2. He fails to explain certain inconsistencies in his results. For example, in his 1912 article (25) certain results lead him to the general statement that scotopic fishes react to the spectrum exactly as do photopic fishes. This is not reconciled with his theory of pigment migration dealt with in the same article, nor with the data reported in defense of this theory. Nor does it agree with results reported in other articles as in 1914 (29) where he found that photopic fishes swam to the yellow-green region more quickly and with fewer exceptions than did scotopic fishes.

3. He fails to recognize certain results reported by Bauer (2) and to answer objections raised by this writer against his work.

4. He excludes "unsatisfactory results" (25).

5. He fails to make control tests with normally negatively phototropic fishes.

6. There are a number of sources of error all of which may have been controlled but probably were not since no mention is made of the control:—

a. Stimulus error. (1) Intensity of light may have varied in different parts of the spectrum because of characteristics of the refracting medium. (2) Thermal cues. (3) Cues from any of the other modalities.

b. Emotional disturbance following movement of fishes from light to dark.

c. Effect of water on the light (variability in amount of water through which light passes before reaching eye of the fish).

Hess's work does seem to indicate that the following statements hold for those species used (all positively phototropic):

1. That response to intensity exists, that it probably dominates response to color if fishes are sensitive to color.

2. That the behavior previously interpreted as indicating the Purkinje phenomenon need not be so interpreted.

3. That those forms of behavior described by Bauer and others as "red-shyness" and "love for blue" do not necessarily indicate color vision since such behavior can be reversed by appropriate manipulation of the intensity factor.

Hess's work has had an important influence in the field of color vision. Parsons (37), for example, states that in his opinion the adverse criticism levelled against Hess has not seriously shaken his position. In our opinion, Hess's greatest contribution was that of calling attention to the difficulty of establishing evidence for color-discrimination and especially to the danger of interpreting brightness-discrimination as color-discrimination.

THE LEARNING METHOD

The learning method has been used even more frequently than the preference

method. Unfortunately, in a large number of investigations the intensity factor has not been controlled (5) (13) (41) (52). Washburn and Bentley (49) made an effort to control this factor. One small fish (*Semotilus atromaculatus*) was trained to take food from red forceps and not from green forceps. The two forceps were always presented simultaneously. The red was for the human (light-adapted?) eye the darker of the two colors. After the association had been established, a red, which by the same criterion was lighter, was substituted without interfering with the habit. As Parsons and others have pointed out, it should not be inferred that the brightness values for colors are the same from one group of animals to another. To be sure that the brightness values of any pair of colors had been reversed, it would be necessary to vary both of them within extremes too great to be obtained by daylight reflected from a pigmented surface.

The practise of varying the intensity of one or both stimuli, keeping the wavelengths constant, has been employed by practically all investigators in their efforts to determine whether differential response has been based on the intensity or the wave-length characteristics of the stimuli. Application of this principle is found in the work of Reeves (39), Schiemenz (43), and others. Goldsmith (18) has employed another method of equating her stimuli for brightness, but one which is faulty. She photographed her colored surfaces and finding that some of them photographed a darker gray than others she attempted to compensate for this by using filters of varying thickness. This method involves the unwarranted assumption that the intensity values of different wave-lengths are the same for the eye of the fish as for the photographic plate.

Reighard (40) noted that gray snappers (*Lutianus griseus*) preferred white bait to blue and blue bait to red. When these were to the human eye matched with grays on color wheels the brightnesses were in the order white, red and blue. Since the choice in one case favored the brighter and in the other the less bright bait, he assumed this choice to have been based upon color. In further experiments he fastened Cassiopea tentacles to baits stained various colors in order negatively to condition the fishes to such colors. The fishes came to refuse harmless bait stained the same color as those previously bearing the tentacles. Varying the brightness of the stains did not seem to affect the behavior of the animals (i.e., if negatively conditioned to red they refused bait stained all shades of red, although they accepted bait of other colors). Reighard concluded that these fishes were capable of color discrimination. Obviously the range of intensities procurable by this method would be limited.

Hess (25) rejects as worthless the work of Zolotnitzky, of Reighard and of Washburn and Bentley on the grounds of unsatisfactory intensity control. To show that brightness was indeed the criterion of discrimination he carried out the following experiments. Minnows and Mugil were fed red chironomus larvae. Then, colored threads of the size and shape of the larvae were glued to the outside of the basin. The fishes disregarded the yellow and white decoys and snapped at the red. This is just what Zolotnitzky found. But Hess went further and tested the animals on various shades of gray, blue and green and was able to find a shade of each to which they responded just as regularly as they did to the red. In further experiments he used imitation larvae made of various chromatic and achromatic papers pasted against paper backgrounds. He was able to produce decoys which were responded to positively when against a dull

white or light gray background. When such a decoy was pasted against a bright red background it was apparently not reacted to at all. When against a pure (?) yellow background there was fastened a decoy of blue paper of a certain brightness the fishes failed to react, although for the human eye the blue differed in hue very distinctly from the yellow background. When against this background a blue decoy of a different brightness was pasted the fishes snapped vigorously. These results are in distinct contradiction to those of other investigators.

Further feeding experiments of Hess (29) served only to strengthen his faith in his previous conclusions. About that time, however, Bauer and Degner (4), using the same general method, came to the conclusion that fish have color vision, though only when they are light-adapted.

The work of von Frisch

Von Frisch (13) repeated certain of Hess's experiments, failing to confirm the latter's results. *Phoxinus laevis* which had been fed for a long time on yellow colored meat snapped at decoys of yellow paper against a gray background. If, as Hess maintained, they snap only at objects which show brightness contrast then a given gray should be found which would have the same brightness value as the yellow decoy pasted upon it at which the fishes would not snap. Von Frisch used a long series of graded grays and did not find one which caused the fishes to refrain from snapping at the yellow decoy. After the fishes had been fed red colored meat for a time they were offered, on a gray background, a small piece of red and a similar piece of black paper. They invariably snapped at the red, never at the black. The same thing happened when the background was black or dark gray. Von Frisch says that this is not the behavior we would expect in an animal whose vision resembled that of the color-blind human. Fishes trained to red would snap at red and at yellow decoys, but not at any other color. Fishes trained to yellow behaved similarly. Both types of fishes snapped at purplish red and both snapped occasionally at greenish yellow but almost never at blue-green or blue.

In further experiments von Frisch used a large number of 8 cm. glass test tubes lined with papers of various colors and with papers of a series of fifty grays ranging from black to white. Shot was placed in the bottoms of the tubes so that they would rest on the bottom of the tank. For a given group of fishes (Phoxinus, usually six tested at a time) six gray tubes and one colored tube were used. Only the colored tube contained food, the others being empty. After several weeks of training the fishes always went directly to the colored tube, irrespective of its position, avoiding the grays. They did this even though the colored tube contained no food. The whole series of grays was used and in no case did a fish confuse any shade of gray with the color to which it had been trained. Then, instead of gray tubes each group was given the choice of red, yellow, green, blue and purple-red tubes in an effort to determine which colors were confused. It was found that red and yellow were quite regularly confused but that blue and green were distinguished from each other and from yellow or red. Purple-red was also confused with red and with yellow. Tabulated numerical results support these conclusions fairly well (a feature the more appreciated since it is infrequently encountered in these studies). Von Frisch holds that these results explain (1) the widespread occurrence of red as a decorative color and (2) the fact of undifferentiated adaptation to red and to yellow backgrounds in Phoxinus.

Burkamp (6) has more recently tested various Cyprinides including Phoxinus in much the same way using, instead of test tubes, trays of various colors and of twenty-four intensities of gray (Fig. 4). The animals were tested in groups of six to twelve. The data, which are reported in tabular form, seem to indicate that the fishes learned to respond positively to the tray in which they had always found food, avoiding, usually, trays of other colors. The trays were so designed as to conceal the food until the fish had definitely made

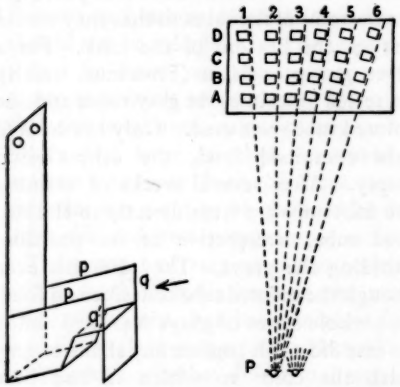

FIG. 4. AT THE LEFT IS SHOWN ONE OF THE TRAYS USED BY BURKAMP. A FISH COULD NOT SEE INTO THE TRAY UNTIL IT SWAM DIRECTLY OVER IT. AT THE RIGHT IS SHOWN THE ARRANGEMENT OF THE TWENTY-FOUR TRAYS

a selection. The position factor was controlled. Intensity was partially controlled by using a confusion series of grays, one of which was supposed (for the fish) to be equivalent in brightness value to the color in question. Olfactory control was apparently attained by using food in none of the trays in the test series although this is not clearly stated. The results, in general, support the findings of von Frisch.

The work of White

White (50) has studied the mudminnow (*Umbra limi*) and the stickleback (*Eucalia inconstans*) using light from a 10-watt Mazda lamp transmitted through gelatine light filters allowing only a narrow band of the spectrum to pass. The fishes were offered food under one color and an unpalatable substance under another. A fish which consistently reacted positively toward a substance offered under the light beneath which it was accustomed to receive food, and negatively under the other light was supposed to have discriminated between the two. Variation in intensity of the light (1.4 to 4.9 c.m.) did not affect the discrimination. Experiments with various shades of gray showed but poor discrimination ability and consequently White is inclined to believe that wavelength difference was the determining factor. The mudminnows apparently distinguished between red and green, red and blue, and yellow and green. The sticklebacks were successful on only the first pair. Realizing that this control of intensity was hardly more adequate than that of previous investigators, she repeated her work (31), using only mudminnows. The following filters were used: red, 660–700 mμ; yellow, 560–600 mμ; green, 510–550 mμ; blue, 400–450 mμ. She states that "the total radiant energy transmitted by these filters was equalized to within about 5 per cent by the addition of layers of neutral-tint film." Unfortunately, we are not informed how these measurements were made, i.e., whether radiometric or photometric methods were used. Furthermore, the range of 5 per cent is not a small one. Otherwise her experimental technique resembled that of her former experiment. She found differential response to the following pairs of colors: red and green, red and blue, red and yellow, yellow and blue. There was no evidence for discrimination between blue and green.

Even were we to grant that White's control of intensity was adequate (that the

lights of the two wave-lengths radiated the same amount of energy), it is quite unlikely that the results reported would persuade Hess that the fishes responded to color. Differential response to differences in wave-length and differential response to color are not necessarily the same. The former involves the factor of luminosity, which varies with variation in wave-length even though intensity remains constant. The latter, supposedly, does not involve this factor. The method used in the studies of White is capable of yielding data on the former problem only. Thus the titles of her articles are misleading.

The work of Reeves

There is a method which can yield data on the latter problem (color discrimination) if we are justified in making the assumption that correction for variation in luminosity can be made by appropriate regulation of the intensities of the lights. Reeves (39), a student of Reighard, has applied it to the study of fishes. The apparatus was essentially a Yerkes-Watson discrimination box modified so that it could contain water. The source of light was a Nernst lamp. Red and blue filters restricted the transmitted light to but a portion of the spectrum. Variation of intensity was produced by the adjustment of the width of a slit placed between the lamp and the filter.

Glass filters transmitting each of the following colors were used: red (572 to 652 mμ), and blue (509 mμ to the end of the visible spectrum). An adjustable slit placed between the lamp and filter furnished the means of altering the intensity. Food was presented for correct choices by means of a mechanical device. In every case the animals were trained toward the blue, the intensity of which was kept constant throughout the work. The red light was varied in intensity "so as to include an intensity equal to the blue." At what intensity of the red its luminosity would be equal to that of the blue for the eye of the fish was of course unknown. The supposition would have to be that by using a very wide range of intensities this intensity would be included. According to the procedure used by Reeves the red was at its maximum during the training series. After the positive response to the blue and the negative response to the red had been fairly well established, the intensity of the red light was gradually decreased. The animal was still fed only before the blue. If the differential behavior of the fish to the two lights were on the basis of color we might expect it to continue in spite of intensity variation. If this behavior were established on the basis of intensity difference it would be expected that at some point the luminosity factor for the red and the blue would be equated for the eye of the fish and the discrimination would break down. If the fish could not respond differentially to color, as such, no amount of training at this point could result in any but a chance distribution of choices for the two lights. In this experiment Reeves used four horned dace (*Semotilus atromaculatus*, Mitchell) and three sunfishes (*Eupomotis gibbosus* Linnaeus). In the case of every subject eighteen correct choices out of a series of twenty were made for at least one degree of red intensity. It thus seems that an association involving discrimination between the two lights was formed in every case, whatever were the characteristics of the stimuli which determined the behavior. There is a surprising lack of uniformity in the records of the various fishes. There was in every case considerable variation in the percentage of correct choices as the intensity of the red light was reduced but this variation was different from fish to fish. We would expect

that within a given species there would be but little variation in the intensity of a red light of the same luminosity as the standard blue light. This did not seem to be the case. The intensity of the red light is indicated only in the width of the slit in mm. In the case of one horned dace the number of correct choices, which had been as high as nineteen out of twenty with a width of 35 mm. (the maximum intensity), dropped to thirteen out of twenty at 0.9 mm. With another dace the low point (ten out of twenty) was reached with 5.0 mm. In the case of the other two dace the percentage correct in a series never dropped below 70. For two of the three sunfish, the low point was reached at 1.8 mm. and at 0.9 mm. respectively. The third sunfish was not given preliminary training at maximum intensity and the results were irregular. But, in spite of these inconsistencies, it may be that the low points do represent failure of the animals to discriminate on the basis of luminosity and that at these points the two lights are equated for this factor. If this is true then we have the ideal situation for the determination of the ability of the animals to discriminate color. It is merely necessary to continue training with these two lights so equated for luminosity. If a discrimination can be established it must be on the basis of color difference.

For some reason this was done with but four of the seven fishes and in three of these cases but one additional series of twenty trials was given at the point where the discrimination broke down. Nevertheless, these few data are of crucial importance, being the only data of their sort in the literature on color vision in fishes. Semotilus "Md," made 13 correct choices out of the first 20 with an intensity of 0.9. Of the next 20 choices with the same intensity "83%" was said to have been correct (perhaps it is meant that 16 of 19 were correct). No further detail as to the order of correct and incorrect choices within a series is given. The statistical validity of the difference between these two short series is not sufficient to warrant definite conclusions. In the case of the second dace so tested, "Yl," the difference is negligible (10 correct choices in the first 20 at 5 mm. and 11 correct in the second 20). In the case of one of the two sunfishes so tested the number correct, having dropped to 11 out of 20 at 0.9 mm., rose to 35 out of the next 40. This difference appears to be significant. For the other sunfish the increase is not appreciable, being from 13 to 14 in 20. If we were to accept data secured by this method as proof for or against color vision we would be forced to say that while the evidence is strong for such in the case of one of the sunfish and fair in the case of one of the dace, data for the other two fishes offer just as good evidence against color discrimination. It could be objected that adjusting the intensity of the red in fairly large steps, as was done, might not necessarily result in the securing of an intensity at which the two colors were perfectly equated. The drop in correct choices might indicate merely that the intensity difference had been so reduced as to render an intensity discrimination difficult and that further training at this point raised the level of the fish's performance. Other experiments of Reeves seem to show that intensity differences to be discriminated by fishes must be relatively large. This throws some doubt on the above explanation of her data. According to an entirely different and perhaps the most plausible explanation the cause of the total or partial failure of the discrimination habit which ordinarily followed intensity changes was merely confusion on the part of the fish. This confusion might well be expected as a result of the changes made in the stimulus situa-

tion to which it had been trained. Similarly, ultimate recovery of the habit might be expected to follow an adjustment to change in the situation. This explanation would render it unnecessary to account for the fact that the break-down in the habit did not always occur with the same intensity of the red light.

Reeves' conclusion that "sunfish and horned dace discriminate light of longer wave-length from light of shorter wave-length" should be accepted as merely tentative, pending further data on the problem.

The work of Schiemenz and others

A recent study made by Schiemenz (44) resembles that of Reeves in that he also kept wave-length constant and varied intensity. The learning required of the fishes (*Gasterosteus aculeatus* and *Phoxinus laevis*) was somewhat different, being rather more like that required of the animal in the experiment of Washburn and Bentley (49). The fishes were trained to accept food from a glass rod. The uniformity of presentation of this rod was insured by the use of a mechanical device. In a training series the fishes learned to leap for the food only when it was presented under the illumination of a certain narrow band of spectral light, and not when illuminated by light from other portions of the spectrum. Having set up this differential response the problem was to determine whether it was based upon color or luminosity differences. Schiemenz attempts to solve this problem by wide variation in the intensities of the lights. Twelve degrees of intensity were used. This differed from the method of Reeves in that he did not determine at what relative intensities lights of different wave-lengths possess the same luminosity value for the fish. Instead he hoped to use such a range of intensities that, were the responses made on the basis of luminosity rather than color, the fishes would some times choose one color, and sometimes the other. Schiemenz reports that he succeeded in training these animals so that they responded positively to all intensities of the color associated with food in the training series and to no intensity of any color not in the immediate neighborhood of this color in the spectrum. By testing the animals on colors differing only slightly from the positive color in wave-length he was able to get an approximation of the acuity of the animal at various points on the spectrum. He reports that their acuity at the blue end of the spectrum was slightly superior to that of man, that at the red end it was inferior. In all test series the rod, whether presented with the positive light or with another light, bore no food. All tests were made on light-adapted fishes in diffuse light.

Three studies, one by Kühn (33), one by Wolff (51) and one by Hamburger (22), differ in method from that of Schiemenz chiefly in the fact that the fishes (*Phoxinus laevis* in every case) were presented simultaneously with a number of areas of light, differing in wave-length, and including one under which the fishes had formerly been trained to feed. The fishes learned to leap from the water for food only in the area where they had previously been fed. Like Schiemenz, these investigators varied the intensities and report that differences of wave-length, rather than of intensity, determined the animals' behavior. In general their conclusions are in accord with those of Schiemenz. Hamburger further offers evidence that, to mixtures of two lights of such wave-lengths as to be complementary (appearing white to the human eye), the minnow responds in the same way that it responds to white light.

The fact that Scharrer (42) was unable to train blinded specimens of Phoxinus to

discriminate between lights of different wave-length suggests that such discrimination is mediated by the eye.

Although Froloff (17) has recently reported data suggesting that *Tinca vulgaris* can distinguish a red from a green light, it is almost certain that the differentiation was based on intensity difference. Froloff was not primarily interested in color reception and admittedly made no effort to use lights of equal energy.

THE PIGMENT CELLS AND COLOR VISION

A type of behavior which has been claimed by some to demonstrate color vision in fishes is the response of the pigment cells to backgrounds of various colors. Sumner (47) and Mast (36) have reported detailed observations of such behavior in the flounders. Both investigators demonstrated that the essential receptor was the eye. Mast concluded on the basis of his observations that color vision in fishes is essentially the same as it is in man. As in the case of practically all studies of color the intensity factor was uncontrolled and thus on this basis we are forced to say that these observations may be indicative of color vision, but are not proof. Presuming, however, that this criticism be waived, there is, nevertheless, a question as to whether behavior of this type could ever establish color vision. To quote from Washburn (48):

> Watson does not think that these observations prove color discrimination in the fish. He says, "Ordinarily, when we say that an animal is sensitive to difference in wave length we mean that such stimuli play a rôle in the adjustment of the animal to food, sexual objects, shelter, escape from enemies, etc.; that such stimuli initiate activity in arcs which end in the striped muscles." Because the changes of color are produced not by such arcs, but by the sympathetic nervous system, Watson thinks color vision not proved: "We can easily conceive," he says, "of mimicry of this kind taking place in an animal whose retina does not contain the physico-chemical substances necessary to initiate response to differences in wave-length." But since the changes of color are induced by differences in wave-length and induced through the retina, we may reply that it does not seem easy, or in fact at all possible, to conceive of the absence of such photochemical substances from the fish's retina.

Whether or not the behavior in question establishes color discrimination is not a matter that can be proven or disproven. It depends upon how one defines that term.

The work of von Frisch and others

Von Frisch (10), who studied this form of mimicry in *Crenilabrus pavo* and *Trigla corax*, reports that when a fish is transferred from one background to another differing from the former in both intensity and color, it accommodates itself first with respect to brightness and then with respect to color. He says that he was able to find a gray paper which appeared to the minnow to be of the same brightness as a certain yellow (or red) paper, for it would accomodate itself to the same brightness (in its own pigmentation) on both. Nevertheless, when the fish was on the yellow paper, expansion of the yellow pigment cells occurred, while this did not happen when the fish was on the gray paper. In another experiment he used as a background first a yellow and then a blue fluid (evidently as a color filter) which were at first so highly concentrated that they appeared black, and then were gradually diluted until they were practically white. In both cases all degrees of brightness were assumed by the fish but the expansion of the yellow pigment cells occurred only in the case of the yellow fluid.

In another experiment (11) von Frisch procured yellow papers of the same color value but of differing degrees of brightness. When transferred from one to the other, the minnows became decidedly brighter, or darker accordingly. Then a gray paper

was chosen which when interchanged with the lighter yellow caused no difference in the brightness of the fish. This gray was assumed to be equated for brightness value with the lighter yellow. When this gray was substituted for the darker yellow, however, a brightening resulted. The two yellow papers were therefore more different from each other with respect to brightness, than were the gray and the lighter yellow. Nevertheless, after prolonged exposure to either yellow paper, there was always expansion of the yellow pigment cells, whereas on the gray background these consistently contracted.

Von Frisch concludes that the minnow possesses a sense of color and recognizes red and yellow as such and not by their brightness values alone, as Hess seems to think probable. In so far as his observations may be accepted as indications of color vision they indicate but a primitive stage of such ability. These fishes reacted only to red and yellow, and to these colors in almost the same way, apparently showing that they were not received as qualitatively different. Green, blue and violet were accomodated to only with respect to brightness.

Hess subjects von Frisch's earlier work, in which the intensity factor was uncontrolled, to the severest criticism. Hess of course holds that all behavior in fishes, apparently determined by differences in wave-length, is actually determined by differences in intensity. Nevertheless, this writer reports some data which certainly uphold von Frisch's view that color mimicry is determined by wave-length differences. Using gray backgrounds of varying intensity values (photometrically determined) Hess found that *Phoxinus laevis* showed no differences in color whether it was on a dark or a bright background, even though the latter were five times as bright as the former. He had previously shown, however, that fishes were sensitive to a difference in brightness of 1.23 to 1.00. In spite of this it is his opinion that any color-matching of which fishes may be capable is the result of brightness rather than wave-length discrimination.

Haempel and Kolmer (21) tested *Phoxinus laevis* Ag. and *Cottus gobio* L. using both transmitted and reflected light. They found little evidence for color mimicry except in the case of minnows which had been taken from the river Wuerm, which has a red bottom. These assumed a red tint when placed in an aquarium lined with red paper and did not so respond when paper of gray or of other colors was used. There is no evidence offered, however, to show that this response was not made on the basis of intensity.

Freytag (8) was able to observe mimicry of intensity but not of color in *Phoxinus laevis*. Reeves (39) objects to his negative conclusions regarding color vision on the grounds that he did not allow the animals sufficient time for adaptation to color.

Connolly (7) has studied the adaptive changes of Fundulus to backgrounds illuminated by spectral lights of different wave-lengths. The lights used were of equal energy as determined by means of a thermopile and galvanometer. He found that *Fundulus heteroclitus* adapted rather slowly, but that after a week's exposure those animals subjected to yellow and red lights were quite distinct from those subjected to blue.

The contention of Hess, that the changes in the brightness values of colors accompanying adaptation are due to the migration of a retinal pigment, receives support in the work of Schnurmann (45). Both these writers contend that data, which apparently indicate color vision, actually demonstrate the effect of retinal pigment. This yellowish pigment, retracted during

dark-adaptation, spreads over the retinal elements upon exposure to light and acts as a differential filter. They conceive its effect to be much like that of yellow tinted glasses upon a color-blind person. In both cases we would expect a far greater absorption of short than of long wave-lengths.

The work of Schnurmann

Schnurmann's data are too extensive to be cited here. He observed the melanophore reactions of light-adapted fishes (*Phoxinus laevis*) to chromatic backgrounds verifying Hess's conclusions (based on different methods) regarding the relative brightness values of different colors. He then tested the brightness values of various colors on a totally color-blind woman with and without the use of a yellow filter. The results showed absorption of a part of the mixed light (gray) and a still greater absorption of a part of the short wave-lengths by the yellow filter. An interesting counter test would have been measurement of the brightness values in dark-adapted fishes, since in such animals the retinal pigment is retracted and thus non-functional.

If such fishes could be tested both with and without the use of a filter of yellow glass, further evidence might be obtained in support of the analogy in function between the glass filter and the retinal pigment. Such tests were impossible, however, since light-adaptation occurred more rapidly than did the melanophore response.

That the retinal pigment seemed to exert no effect in the decoy tests (2.4) is explained by the fact that those rays which enter the eye at right angles to the back surface of the retina (in other words, those which come from a small object which is fixated,) are not absorbed by the pigment because of its peculiar structure.

Schnurmann makes this statement concerning the reactions of the chromatic pigment cells in Phoxinus: "During three and one half month's investigation on minnows from the Ulmar region, I was unable to discover any yellow coloration on yellow, red or orange backgrounds which I could not also get on differently colored or achromatic background of all degrees of intensity." These fishes assumed a yellow coloration in darkness which they lost upon increase in illumination.

The fishes from the Munich region, on the other hand, regularly became yellow over yellow, orange and, to a lesser extent, red backgrounds. The latent time of yellow matching was much longer than that of brightness matching, requiring from one-half hour to five hours. Disappearance of the yellow coloration was just as slow. In deep basins the yellow coloration usually did not occur. Supposedly this was because the effect of the yellow ground was not continuous on the dorsal side of the retina. The matching was only relative, not absolute, the coloration being the same whether the background was yellow, 120 degrees, or orange, 37 degrees. The same fishes which became yellow on a yellow background (those from the Munich region) also became yellow if held in an absolutely or very nearly dark place. The three conditions under which the xanthophores expanded, therefore, were:—

1. Absolute darkness (no rays for the yellow pigment to absorb).

2. Very weak light (the yellow pigment being retracted, absorbed but few rays).

3. Yellow or reddish-yellow background (the yellow pigment having few rays to absorb inasmuch as the background reflected only long-waved rays. This refers to the dorsal retina only).

In short, when the pigment of the dorsal retina is absorbing light of short wavelength the yellow pigment of the skin con-

tracts. When the pigment of the dorsal retina is not absorbing such light, the yellow pigment of the skin expands. Thus there may be a reflex connection between the retinal pigment, in its activity or non-activity, and the pigment cells of the skin. This separation of the reflex connections governing brightness-matching from those governing color-matching, corresponds with the differences in latent time, if we imagine that it requires some time for the chemical changes in the retinal pigment to take place..

There is another conception of this matter of matching, which would account for the behavior of Phoxinus without implying color vision. Melanophore contraction is determined by equalization of the amount of light striking the retina in all its parts. We would get brightening, therefore, in complete darkness, in deep water where the axis of the retina is being continuously changed, and on light backgrounds which reflect most of the light striking them. Expansion of the melanophores occurs when the dorsal retina does not receive the same amount of light as the ventral or lateral retina. Xanthophore contraction, on the other hand, is determined by non-equal illumination of the various parts of the retina. On a blue background, for instance, the dorsal retina is exposed mostly to short wave-lengths which are to a great extent absorbed by the retinal pigment. On a red or yellow background practically none of the rays reflected from the bottom to the dorsal retina are absorbed whereas the short waves coming from above are absorbed. Thus equalization of stimulation causes xanthophoric expansion. So in darkness or near darkness there is equalization and yellow coloration.

Schnurmann's observations and interpretations are important, not merely in themselves, but because they stress the fact that there may be an adequate explanation of the matching of chromatic backgrounds which does not involve the assumption of color vision.

OTHER EVIDENCE

Hess has made a study of another unlearned response as it is related to stimulation by colored light. The pupil of the eye of most fishes responds to an increase in intensity of illumination by contraction. Hess has recorded these responses both by photography (25) and by means of a measuring device, the pupilloscope (30). By this means he has obtained data concerning the relative brightness values of light from different parts of the spectrum but of (supposedly) equal intensity. He asserts that the results obtained corroborate his other work, indicating that these brightness values are the same for fishes as for the totally color-blind human eye.

A form of evidence, or rather argument, that has been used for and against the existence of color vision in fishes relates to the utility of such ability should it exist. Hess maintains that monochromatic light, especially of the longer wave-lengths, penetrates the water to such a short distance that in most cases there would be no colors for fishes to see even though they had color vision. Von Aufsess (1) has shown that in 8 meters of water (from Bavarian lakes) only 1/60 of the red waves (600 mμ) is still present. At a depth of 20 meters only 1/10,000 remains. Hess himself made experiments on this problem using Hering colors. The papers were protected against water by celluloid. At a depth of 2 meters, in bright daylight the red looked a dull brown; at 3.6 meters the orange looked brownish yellow though the yellow and blue could still be recognized clearly; at 4.6 the red and orange could not be seen as such but as gray;

at 5.6 meters none of the colors could be recognized. One sample of each color was tested against a black and one against a white background. The following question still remains open: Is it merely the depth of water through which the light passes downward that destroys certain of the wave-lengths and thus renders the colors invisible, or is not also the quantity of water through which the colored paper is seen a factor? Our interest is in the way these papers might look to the fishes. Hess should have observed their appearance with his eye submerged to their level. But even though it could be conclusively demonstrated that monochromatic light did not penetrate to any great extent into the normal environment of a fish, this would not be proof that the animal was color-blind. There are other forms of stimulation, not normally found in the environment of many animals, which, nevertheless, when presented, are effective stimuli.

In support of color vision, the point has been made that the coloration acquired by fishes during the mating season must have developed for a "purpose" which could not be fulfilled if the fishes were color-blind. Von Frisch names a number of fishes which breed at night or at such depths that color would be invisible. All of these fail to acquire bright hues during the mating season. He also gives a list of species which, mating under conditions where color would be visible, acquire such coloration. Hess notes one exception to this correspondence of coloration and habit (the Saiblinge). This is not sufficient grounds, according to von Frisch, for rejecting the evidence of the other thirty-odd species.

Consideration of the many and conflicting data on the subject has led the writer to conclude that some fishes, at least, do respond to color as such. Anglers, with their kits of flies of all hues, would scoff at any other conclusion. It is very probable, however, that the capacity to discriminate colors is far less developed in some species than in others. There may also be age differences. Nine-tenths of the experimental work in the field would bear repeating. Especially the investigations of Hess, which have often yielded data out of harmony with most other workers, should be repeated carefully. Many of his techniques are most ingenious and should furnish admirable starting points for truly conclusive experimentation.

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NEW BIOLOGICAL BOOKS

The aim of this department is to give the reader brief indications of the character, the content, and the value of new books in the various fields of biology. In addition there will frequently appear one longer critical review of a book of special significance. Authors and publishers of biological books should bear in mind that THE QUARTERLY REVIEW OF BIOLOGY *can notice in this department only such books as come to the office of the editor. The absence of a book, therefore, from the following and subsequent lists only means that we have not received it. All material for notice in this department should be addressed to Dr. Raymond Pearl, Editor of* THE QUARTERLY REVIEW OF BIOLOGY, *1901 East Madison Street, Baltimore, Maryland, U. S. A.*

BRIEF NOTICES

EVOLUTION

THE FORMENKREIS THEORY AND THE PROGRESS OF THE ORGANIC WORLD. *The Re-Casting of the Theory of Descent and Race-Study to Prepare the Way for a Harmonious Conception of the Universal Reality.*
By O. Kleinschmidt. Translated by the Rev. F. C. R. Jourdain. H. F. and G. Witherby
10s. 6d. net $5\frac{1}{2}$ x $8\frac{3}{4}$; 192 *London*

This is a distinctly disappointing book. After a careful reading, we remain unable to give any clear statement either of the meaning the author attaches to the term *Formenkreis* or to the theory itself. As far as we have been able to make out, the *Formenkreis* is a taxonomic unit used by the author in preference to the genus or the species; but there is nothing in the way of a clear statement of just what determines his classification, and how it differs from that of other taxonomists. As regards his theory, the case is a little clearer. He appears to hold that the *Formenkreis* is the largest unit within which relationship by descent can be shown to hold. He denies that one *Formenkreis* can arise from another; and while he is a trifle vague on the point, he seems to lean toward the independent origin of different forms.

Whether there is any great merit in the author's ideas we cannot say; because, as already indicated, we are still in the dark as to just what these ideas are.

RATIONAL EVOLUTION (*The Making of Humanity*)
By Robert Briffault *The Macmillan Co.*
$3.50 $5\frac{3}{4}$ x $8\frac{1}{2}$; 302 *New York*

A book for your pastor, if he can read. The author dislikes Christianity considerably, and argues with much plausibility that Arabic culture was the real source of modern culture. We suspect that he overestimates the Arabs, as we are sure that he underrates Aristotle. But with all the statements which the reader will regard as erroneous or doubtful, the book is well worth reading.

ADAPTIVE MODIFICATIONS IN THE WOODPECKERS. *University of California Publications in Zoology, Volume 32, No. 8.*
By William H. Burt
University of California Press
$1.00 7 x $10\frac{3}{4}$; 70 (paper) *Berkeley*

A detailed anatomical account of the

modifications of the skeletal and muscular systems of the various species of woodpeckers, which are regarded as adaptations of their habits of life.

The adaptive modifications in the various structures such as the tail feathers, pygostyle, or skull show a positive correlation with the habits of the birds. This correlation is repeated many times in the group, and because of its recurrence the evidence is strengthened for considering that the environment, likely, at least in part, through natural selection, has been an important factor in modeling the group as we see it today.

GENETICS

A NEW THEORY OF HEREDITY

By George A. Gaskell *C. W. Daniel Co.*
2s. 6d. 4 x 6½; 93 *London*

The theory advanced in this book seems, so far as we know, to be new; whether it is true is another question. A few quotations will allow our readers to judge for themselves:

The Discovery of the actual method of the mental and vital transmission of influence for the production of organisms. First, there is the contacting of the psychic nature with the physical, resulting in the formation of a mass of watery and nutritive 'living matter' in which bioplasts are endued with sensation, desire and hunger, and thereby *guided* mentally in the use of physical forces and particles of matter required in the construction of organisms. The microscope reveals the process.

Notwithstanding the general belief in parental heredity, no evidence can be found for it. Such evidence as there is relating to conception and the process of growth, directly contradicts the idea of inheritance coming from or through parents. Proof of the transmission by parents to offspring of acquired or any other characteristics is entirely wanting.

A warmed hen's egg may produce a chicken in an incubator after its parents have been killed and eaten, which shows that parents have nothing whatever to do with the heredity of their species.

A swan or albatross must use up enormous power in flying, yet the muscles of its wings are not torn, although the bird may be for hours in the upper air. This source of force we may anticipate will become accessible to human beings when man investigates his own mental and psychic nature guided by a *true* theory of life, free from the misleading errors of the present variety of authoritative theories.

This force, which may be called provisionally 'etheric force,' would be very welcome for aeronautics, and its accessibility is likely to be accomplished in no great length of time by the application of psycho-mental methods of research into the causes of normal and abnormal phenomena of life and mind, and the relation these phenomena must have to heat, electricity and currents in the ether.

THE LABORATORY MOUSE. *Its Origin, Heredity, and Culture.*

By Clyde E. Keeler *Harvard University Press*
$1.50 6 x 9; viii + 81 *Cambridge*

A brief and attractive summary of data on the mouse, with particular reference to its use as material for genetic experiments. There are chapters on the geographical distribution of the house mouse, on the antiquity of the fancy mouse, on unit characters, on normal and on abnormal inheritance, on laboratory breeding, and a bibliography of 184 titles.

L'HÉRÉDITÉ. *Deuxième Édition, Revue et Augmentée.*

By Émile Guyénot *G. Doin et Cie*
32 francs *Paris*
4½ x 7; vi + 470 (paper)

This is one of the best accounts of the present state of our knowledge of genetics which has come to our attention. The exposition is clear and logical, the choice of examples excellent, and the documentation ample.

GENERAL BIOLOGY

JORULLO. *The History of the Volcano of Jorullo and the Reclamation of the Devastated District by Animals and Plants.*

By Hans Gadow *The Macmillan Co.*
$3.00 (U. S. A.) *New York*
7s. 6d. (England)
Cambridge University Press
Cambridge
5⅜ x 8½; xviii + 100

The eruption which built up the volcano of Jorullo in Mexico, began in 1759 and continued intermittently for several years. Prior to this time not only had there been no sign of volcanic activity but the region, an area of about fifty square miles, had been one of great fertility. In fact, the name Jorullo, meaning Paradise, had been given to the district. With the series of eruptions, an area of at least five square miles was completely buried in mud, sand, and lava, while a much larger area suffered widespread destruction of plant and animal life. Ashes fell as far as 125 miles distant. Within 90 years of the catastrophe the flora had practically regained the lost ground, except in those places where the lava covered the surface.

Gadow visited the region in 1908. At that time he found every available stretch of level ground, except the Malpais (lava fields) under cultivation. The slope of the volcano was densely wooded, although as late as 1872, the vegetation reached scarcely half way up and was very thin. The author deals with the story of the eruption as it has been recorded by various individuals and the history of the invasion of the devastated region by plant and animal life as he found it. He found that animal life was restricted almost entirely to reptiles and amphibia. Even so, considerable exploring of the unaffected region was necessary to trace the lines of invasion. The work includes a map showing the geological formation of the volcano and the surrounding region. Philip Lake contributes an editorial preface and there is a prefatory note by A. C. Seward.

THE INTERPRETATION OF DEVELOPMENT AND HEREDITY. *A Study in Biological Method.*
By E. S. Russell *Oxford University Press*
$5.00 5⅜ x 8½; 312 *New York*

In this interesting book Dr. Russell begins with a historical sketch of theories of development and heredity from Aristotle to the present day, and then develops a theory of his own, to which he applies Ritter's name 'organismal.' This emphasizes the functional unity of the living thing. While analysis is a necessary process in science, it always leaves something out of the picture. He is therefore critical of particulate theories, such as that of the gene. The evidence that the nucleus alone determines development and heredity is defective. Rather the evidence is that the nucleus and cytoplasm interact in the process.

The book is well worth reading. If it does not convince the particulatist of the error of his ways, at least he will profit by this critique of his foundations.

DAS LEBENSPROBLEM *im Lichte der modernen Forschung.*
By O. Kestner, L. Rhumbler, J. von Uexküll, L. Weickmann und P. Mildner, G. Wolff, R. Woltereck. Edited by Hans Driesch with Foreword by Heinz Woltereck.
Quelle und Meyer
20 marks 6¾ x 9¾; xi + 461 *Leipzig*

This collection of essays deals with the origin, the nature, and the conditions of life. It is written with true German *Gründlichkeit;* for instance, Professor Kestner's article on The Functions of Life would serve very well as an introductory text on physiology. In the last article Professor Driesch rehearses his reasons for concluding that the individual must be identified with the entelechy.

PHILOSOPHY OF A BIOLOGIST

By Sir Leonard Hill

Longmans, Green and Co.

$1.40 $4\frac{1}{2}$ x 7; viii + 88 *New York*

In this readable little book a distinguished physiologist gives us his synthesis of modern science. That the physiological section of the book is the most colorful and interesting is perhaps natural. His summing up is

> that modern science has brought us to the conception of a power eternal, infinite, unknowable, "the power behind the sun" of the Egyptian king Akhnaton, energizing all in the universe, the dead no less than the quick; a power equivalent to the purest conception of God stripped of all dogma and superstition; a power in all and through all, whence we came, of which we are a part, and whither we return after death; a power active in all atoms of matter composing the nebulae, the stars, the dust and the living cell; a power determining every action and reaction in the eternal evolution of the universe, the earth and life upon earth. The mystery of a living cell is, then, neither less nor greater than that of a drop of water; ceaseless reactions to the environment occur in both. The author suggests, too, that the recent developments of neurology, such as the study of reflex actions by Sherrington and conditioned reflexes by Pavlov, by lifting the veil which has hung over the reactions of the nervous system, are becoming of fundamental importance in the guidance of education.
>
> Science, having dispelled the superstitions of past ages, should keep us to a pure faith and free from any modern revivals of witchcraft. The great conjurors have never been excelled by the manifestations of spiritualists, and the supposed messages of those who have passed over are characterized by a triviality which corresponds with the intellects of charlatans who act as mediums. Such a book as the *Road to Endor* was of great service in showing how clever men confessedly tricked a whole community by methods which lead the credulous to belief in spiritualism.
>
> While metaphysics, creeds, spiritualism, remain barren, the exact observations and operations of scientific research, applied, not to war at the behest of ignorant governments, but to peace, work wonders in saving life and extending happiness.

A SURVEY OF NATIONAL TRENDS IN BIOLOGY

By Edward J. v.K. Menge

The Bruce Publishing Co.

$2.00 $5\frac{1}{2}$ x $7\frac{5}{8}$; xi + 156 *Milwaukee*

A set of lectures prepared for the National University of Cordoba (Argentina), dealing with the outstanding biological theories and workers of the present time.

HUMAN BIOLOGY

TABLEAUX D'HISTOIRE GÉNÉRALE.

Présentation Synchronique des Principaux Événements Contemporains à travers les Siècles. Politique, Religions, Philosophies, Lettres, Arts, Sciences, Découvertes, Inventions, Institutions.

By J. Berthier and C. Lauvernier

Société Mercasia

160 francs net *Paris*

$10\frac{3}{4}$ x $14\frac{1}{4}$; 43 double page tables + 6 pages index

Chronological outlines of history are among the most useful of all reference books. Such a work is the equivalent of a digest of the daily newspapers as they appeared (or would have appeared if there had been any) day by day since the beginning of records. This is the form in which any sensible man wants the record presented. Historians have almost invariably confused and befuddled the common man (and irritated the scientifically minded man as well) because they have felt it imperative in their manner of presenting the subject to depart from the newspaper's simple chronological record of what happened day by day.

The present volume is extremely well done. A double page is devoted to a century of time, beginning with 600 B. C. and ending with 1900 A.D. On such a double page is recorded, against a horizontal time scale, the flow of events in the fields of politics, religion, philosophy,

letters, arts, sciences, and other human oddments. In the later centuries, where one double page is not enough to take care of all these classes, the century is reduplicated as many times as necessary until all subdivisions have been adequately treated. The result is superb. There is naturally somewhat heavy emphasis upon French events and personalities, but after all the French have been and are a highly important branch of mankind—perhaps the most highly civilized human beings yet evolved—and any possible overemphasis of their achievements in this volume is not at the expense of other peoples.

We recommend this book unreservedly to our readers.

WILLIAM STEWART HALSTED. *Surgeon.*
By W. G. MacCallum
The Johns Hopkins Press
$2.75 5½ x 8¼; xvii + 241 *Baltimore*

The old saying that genius is an infinite capacity for taking pains is nowhere truer than in the case of the great surgeon. But this is only half the story. We all know people who take infinite pains over their work and yet produce a hopelessly mediocre result. The genius has the further gift of knowing what to take pains over and what kind of pains to take. These two qualities of fertility of mind and meticulous attention to detail were strikingly exemplified in Dr. Halsted. In his biography Dr. MacCallum has drawn a vivid picture both of the great surgeon and of the elusive but intriguing personality. Perhaps the best summing up of Halsted as a surgeon is that which he quotes from Leriche.

> For those who have visited the Johns Hopkins Hospital, two things stand out: Halsted has created a method in surgery and he has inspired disciples. It is this that gives his clinic such vivid originality, and when one has seen intimately that admirable organization one understands why Baltimore has rapidly become the cradle of contemporary surgery in the United States.
>
> The method of Halsted rests primarily on the biological idea, for those in Baltimore are the surgical inheritors of the spirit of Claude Bernard. It is taught there that surgery should be above all an experimental science. It is on experiment that surgical pathology should lean constantly if it is to progress, and on the other hand experiment should precede and follow every new operative attempt. Surgery is only applied biology . . . In Baltimore the fusion of surgery and physiology is intimate. The education of the students is above all biological, and the future surgeons are trained in a laboratory of experimental surgery in contact with living beings, and not in a dissecting room.
>
> Halsted has established the principle that the surgical operation, to attain all that can be expected of it, should respect life, not only of the individual but of the tissues. It must not introduce the least infection and must not traumatise the tissues. On the other hand nothing in the operation can be left to chance. There can be nothing approximate in experimental biology, and every operation should be a physiological experiment in which the desired result should be obtained with mathematical exactness.

THE BOOK OF MY LIFE. (*De Vita Propria Liber*)
By Jerome Cardan. Translated from the Latin by Jean Stoner
E. P. Dutton and Co., Inc.
$3.50 5½ x 8; xviii + 331 *New York*

Cardan was a genius, beyond question. He had many of the accepted *stigmata*. No one can doubt this who reads Henry Morley's delightful biography. As is not uncommonly the case with superior men Cardan excessively irritated lesser persons, not only contemporaneously but in perpetuity. He had to wait a long time before a really sympathetic biographer appeared in the person of Henry Morley. Now, three quarters of a century after the appearance of Morley's life, there appears to be a considerable re-

awakening of interest in old *Girolamo*, of which the present volume is an evidence. What this is due to is not easy to say—perhaps the New Humanism is responsible in part, and perhaps the present widespread interest in biography plays a part.

In any case, whatever the reason, it is good to have this fresh translation of Cardan's most famous book, the *De Vita Propria Liber*, which has never before been published *in toto* in an English version. Morley's characterization of the book is the best possible description of it, as "no autobiography, but rather a garrulous disquisition upon himself written by an old man when his mind was affected by much recent sorrow."

The present translation is an honest, painstaking one, perhaps more remarkable for a rather literal sort of accuracy than for literary grace. Everyone interested in human biology will want to read the book and have it on his shelves for permanent reference. If the publisher and translator want to have blessings (and probably not cash) showered down upon them they will go ahead and bring out a complete translation of Cardan's *Opera Omnia*.

GROWTH OF CHILDREN IN HAWAII; BASED ON OBSERVATIONS BY LOUIS R. SULLIVAN. *Memoirs of the Bernice P. Bishop Museum, Volume XI, Number 2. Bayard Dominick Expedition Publication Number 17.*
By Clark Wissler

Bernice P. Bishop Museum
$2.00 *Honolulu, Hawaii*
$9\frac{1}{2}$ x $12\frac{1}{2}$; 151 (paper)

The collection of anthropometric measurements and of data on qualitative characters of the Hawaiians was one phase of the major problem of studying the origin and migration of the Polynesian people, an investigation carried on by the Bayard Dominick expedition. Dr. L. R. Sullivan had charge of the Hawaiian work. He had completed the task of gathering the material in 1921 but had not put it in usable form before his death occurred. To Dr. Clark Wissler fell the duty of assembling the tabulations for publication and of writing the descriptions and comparative statements. Records were obtained on about 1000 pure Hawaiian adults, 2000 mixed Hawaiian individuals and 9000 school children ranging in years from 5–19 and representing the following groups: Hawaiian, Chinese, Japanese, North European, South European, Korean, Filipino, Hawaiian-Asiatic, Hawaiian-North European, Hawaiian-South European, and Hawaiian-Asiatic-European.

The report includes descriptions of the measurements taken and 67 tables exhibiting the statistical data collected, and a literature list.

CHILD LABOR IN NEW JERSEY. *Part 3. The Working Children of Newark and Paterson. U. S. Department of Labor, Children's Bureau Publication No. 199.*
By Nettie P. McGill

U. S. Government Printing Office
15 cents *Washington*
$5\frac{3}{4}$ x $9\frac{1}{8}$; v + 94 (paper)

In this survey of child labor in New Jersey two bulletins have previously appeared on (1) employment of school children and (2) children engaged in industrial home work. The present bulletin, dealing with the cities of Newark and Paterson, gives an exhaustive statistical survey of progress in school, grade completed, and age at date of leaving school, occupation and industry, wages, unemployment, steadiness at work, etc. Among

the results which this study yielded are the following:

Newark and Paterson working children had been younger on going to work and had had less schooling than children in many other cities who go to work before the age of 16. The great majority had less than an elementary-school education.

Discontinuing school and going to work was not associated with the loss of the father in the case of either girls or boys.

The great majority of the children in both cities became semiskilled factory operatives.

The proportion of those who had worked less than a year who could be classified as definitely unsteady was very large, but only a small percentage of the workers in both cities who had been at work as long as a year would be so classified. Children who had been 15 on first going to work seemed to have had a somewhat wider choice of employment, less unemployment on the whole, and slightly better wages, except in the case of Paterson girls, than those who had been younger. Children from the lower grades were more likely to take factory employment, those from the higher grades office and sales work.

RACE MIXTURE. *Studies in Intermarriage and Miscegenation.*
By Edward B. Reuter *Whittlesey House (McGraw-Hill Book Co., Inc.)*
$2.50 5⅜ x 8; vii + 224 *New York*

This book consists of a group of papers which have been delivered before sociological societies. Most of them have appeared elsewhere in print. Each paper forms a complete study in itself but they are all on the same general subject, race mixture, and throughout all of them there runs the general thesis that: "The physical differences between races, particularly skin color, is made the basis for caste distinction and differential treatment which give rise to psychological and sociological phenomena that are in no sense racial and may be understood only in social terms."

After a general discussion of civilization and the mixture of races the author devotes much space to the amalgamation of the black and white race, particularly in this country, and the mental achievements and social status of the product of this mixture. There are chapters on sex distribution in the mulatto population, the legal status of racial intermarriage, the superiority of the mulatto, the hybrid as a sociological type, etc. He recognizes the superior achievement of the hybrid but in the analysis of this superiority finds that it can hardly rest in an improvement due to blood mixture. Rather it lies in the "cultural contacts and personal mobility consequent upon the mixed ethnic origin." The book contains bibliographic references and is indexed.

CHINESE CIVILIZATION
By Marcel Granet *Alfred A. Knopf, Inc.*
$7.50 6 x 9¼; xxiii + 444 *New York*

The writer has attained a remarkable insight into ancient Chinese civilization from a thorough exploration of original sources. He has presented much more than a documentation of events, for he reveals a rare comprehension of the complex phenomena of social organization in ancient China.

The most interesting chapters of this book are those portraying Chinese "society," in particular the details of public and private life. The keynote of this civilization in its highest development was etiquette.

There is among the Chinese a mastery of their sensibilities that is simply extraordinary. Decorum, etiquette have repressed all spontaneous display and resulted in an at least apparent drying up of feeling. The expression of the emotions—and notably of mourning—has an entirely conventional character.

Public life is one continuous parade governed by the most elaborate rules. Whether or not this is as true for the masses of people it is hard to say, since

little is known. But the history of the upper classes shows that

> During the long centuries of its ascendancy the Chinese acquired precious virtues through their feudal discipline. They recognized the merits of formalism, of regulated actions, of ready-made formulas. They understood the moral value of conformity. As an essential duty they laid down the practice of the most entire and genuine loyalty: they had the wisdom to define it by a formal adhesion to a whole collection of consecrated conventions of established hierarchies, of good traditions. They made sincerity and honour the fundamental principles of their conduct and their thought. They codified with strictness the practice of these virtues, and when they decided to devote their lives to the worship of etiquette, they succeeded in avoiding the uneasiness of mind which may result from anarchical pursuit of the just and the true.

In private life also everything is dominated by rules. Conventionalized conduct and respect are substituted for intimacy and affection to a degree that would astound westerners. "Regulated on the model of court assemblies, domestic life forbids all familiarity. Etiquette rules there and not intimacy."

The development of this highly cultivated taste for decorum from the instinctive desires of contest, and "passion for prestige," arouses ones admiration. Thus it happened that battles became highly refined and cultured, where each side refrained from being discourteous to the extent of beating the other badly up. All relations were fixed by custom, and the ideal striven for was one of "strained politeness."

> Finally in political life where the stage is reached of advocating the principle of government by history, it appears that it is claimed as sufficient for everything to follow solely the virtues of a traditionalist conformity. So, at the moment when, towards the beginning of the impirial era, Chinese civilization seems to arrive at a point of maturity, everything cooperates to bring to light the reign of formalism.

The author, besides being an historian, is undoubtedly a real artist. He gives picturesque descriptions of the peasant, his life in the fields, his dwellings, his attire, his habits of life during the various seasons.

Equally good descriptions are given of court life, the feudal lords and family life of the upper classes. Granet's ability to reconstruct this civilization from a tangle of legends, sayings, formulae, songs and records is deserving of great credit.

A TRAVELER IN INDIAN TERRITORY. *The Journal of Ethan Allen Hitchcock, late Major-General in the United States Army.*
Edited and Annotated by Grant Foreman
The Torch Press
$5.00 6¼ x 9½; 270 *Cedar Rapids, Iowa*

General Ethan Allen Hitchcock, a grandson of the famous Ethan Allen, was a graduate of West Point in 1817. During the Florida wars he distinguished himself by his great tact and fairness in dealing with the Indians. In 1841 he was sent to the Indian Territory to investigate the scandals in connection with the Act which caused the Indian tribes of the east to be removed to the western reservation. Not only was the report of this investigation never allowed to come before Congress, too many friends of the Administration having been involved in the famous transaction, but it disappeared completely from the government files. General Hitchcock kept copious notes, however, not only on his criminal investigations but on all that came within his notice. Domestic scenes, habits and customs of the tribes that he visited, their amusements, quarrels, religious beliefs and tribal councils all interested him. These notes are now published in the form of a journal. Undoubtedly, General Hitchcock did not intend them for publication, at least in their original form, for he included

many details concerning his own movements which could have little interest for the reader. But his records are well worth reading for the vivid picture which they give of Indian life as it existed ninety years ago. In an appendix appear several letters written by General Hitchcock which were discovered by the editor after the journal had gone to press. The work includes a map of the Indian territory and an index.

GENETIC STUDIES OF GENIUS. *Volume III. The Promise of Youth. Follow-up Studies of a Thousand Gifted Children.*
By Barbara S. Burks, Dortha W. Jensen and Lewis M. Terman. Assisted by Alice M. Leahy, Helen Marshall, Melita H. Oden.
Stanford University Press
$6.00 *Stanford University, Calif.*
$5\frac{3}{4}$ x $8\frac{5}{8}$; xiv + 508

This volume contains the results of a follow-up study of the gifted children reported on in volume I of these studies. Part I of this volume is devoted to statistical analysis and discussion of the performance of the children on various tests and their achievements thus far in their career. Part II is devoted to case studies, and Part III to a study of juvenile literary production, with an attempt to derive a scale for rating the literary merit of such work.

We were somewhat surprised and perplexed in reading the chapter on the retests of intelligence. It was found that those children who took the Stanford-Binet test, and whose I.Q.'s could consequently be determined showed a lower average I.Q. on retest. The possible reasons for this change are discussed and debated at length; but there is no indication that such a change might be the natural result of an imperfect measuring instrument. It would appear obvious that if we selected a group of high I.Q.'s on the basis of some test, and then retested by some other test, we should expect a lowering of the mean of the group. But we have found no suggestion of this in the book.

BIRTH REGISTRATION AND BIRTH STATISTICS IN CANADA.
By Robert R. Kuczynski
The Brookings Institution
$3.00 6 x 9; xii + 219 *Washington*

A book of interest to the vital statistician. Canada is the only country in the world that can boast of a continuous series of birth records covering three hundred years. This, however, is confined to French Canada and is due to the Catholic clergy who in early colonial times inaugurated a system of registration of births, marriages and deaths. French Canadian records show the highest fecundity that has ever been observed in any country. That fecundity, however, has decreased considerably in recent years. In English-speaking Canada birth registration has been no more satisfactory than it has been in the United States. The author devotes considerable space to a discussion of the struggle which the provincial governments have had with clergymen, physicians, civil officials and parents to secure adequate registration and the efforts that have been made to obtain a unification of vital statistics in the Dominion. Included in the report are many tables dealing with birth statistics and an index.

YOUR CHARACTER FROM YOUR HANDWRITING. *A Guide to the New Graphology.*
By C. Harry Brooks
William Morrow and Co.
$1.75 5 x $7\frac{1}{2}$; 207 *New York*

Graphology is trying to acquire the

dignity of an exact science like chemistry or physics. The author explains about all this in this little book, which is a brief outline of the more copious work of Robert Saudek, one of the world's leading authorities on graphology. The chief accomplishment of this book, however, is to show that character is only one of a number of equally important factors which make for different types of handwriting. And while there are a number of excellent methods prescribed for judging handwriting, one feels that it is rather futile to put too much confidence in them since there are so many elements concerned which are difficult to determine from observing a script, such as age, sex, writing material, etc.

THE BRONZE AGE.
By V. Gordon Childe *The Macmillan Co.*
$3.50 *New York*
$5\frac{1}{8}$ x $7\frac{1}{2}$; xii + 258 + map

A careful study of the prehistoric bronze tools, weapons and ornaments of Western Europe and of the pottery and other remains associated with them. The Bronze Age marked not only an advance in technical knowledge but the beginning of industrial specialization. Any hunter or farmer could make a flint knife or arrow-head in his spare time, but mining, smelting, forging and casting were more complicated arts, whose mysteries were handed down in special guilds. Moreover, the limited distribution of copper and tin ores involved wider and more regular trade relations than had been necessary in the Stone Age. The use of bronze began probably in either Egypt or Sumer and spread thence to Europe. Various cultural groups may be distinguished, but their identification with the racial groups of later times is as yet uncertain.

DISEASE AND THE MAN.
By George Draper *The Macmillan Co.*
$4.50 $5\frac{1}{4}$ x 8; xix + 270 *New York*

A book which should interest a wide circle of readers. It continues along the lines of the author's earlier *Human Constitution*, but also discusses the psychological relations of constitution and disease. The facts presented and the conclusions suggested are interesting and sometimes surprising; they are, of course, to a considerable extent preliminary, but they indicate that much is to be learned by continued study along the lines that Dr. Draper has been following.

THE EDUCATION OF MEXICAN AND SPANISH-SPEAKING CHILDREN IN TEXAS.
By Herschel T. Manuel
The Fund for Research in the Social Sciences
$1.25 net 6 x 9; ix + 173 *Austin, Texas*

The author considers this report little more than a preliminary survey. His contribution, however, is of value in opening up the field and pointing the way for future work. Some of the salient points which he brings out are as follows:

About 13 per cent of the total scholastic population in Texas is Mexican. Mexican children come from homes representing all degrees of economic and social status from the highest to the lowest. The prevailing picture, however, is one of under privilege —often extreme. Among the factors responsible for the generally unfavorable standing of the Mexican children in Texas schools are the following: (a) lack of knowledge of the English language; (b) the low social-economic status and cultural level of a large proportion of the population; (c) inferior school opportunities; (d) unsuitability of measuring instruments to reveal clearly the extent and nature of differences in racial groups. Nearly half of the Mexican children who are in school at all are in the first grade, nearly $\frac{3}{4}$ in the first three grades and only 3 or 4 per cent in the high school. In colleges and universities of Texas, the number of Mexicans is less than $\frac{1}{3}$ of 1 per cent of their scholastic population.

The author found that in some localities there was wide spread discrimination against Mexican children in the provision made for their public education. No doubt one of the reasons for this is the hygienic conditions among the children of the lowest social level. The report includes a large number of statistical tables, distribution maps and a bibliography. There is no index.

THE PSYCHOLOGY OF ACHIEVEMENT.
By Walter B. Pitkin *Simon and Schuster*
$3.50 5¼ x 7¾; xi + 502 *New York*

We are a little disappointed to find a stylistically clever but nevertheless superficial piece of writing coming from an author, some of whose works we had heretofore rather admired. But the book does contain some gorgeous contributions to human biology.

> Babe Ruth's eyes are the best of five pairs. His ears are the best of five pairs. So his combination of eyes and ears is the best out of twenty-five men. His general attention is the best out of one hundred men. So the combination of his eyes, ears, and general attention is the best out of 2,500 citizens. His nervous ability is the best out of 500 men. So the combination of this with the three preceding sets of traits, make him the best out of 2,500 x 500, or 1,250,000 people. And we still have to reckon with his amazingly high resistance to fatigue and his muscular strength.
>
> Underneath all of these we find, as the solid foundation of his physical genius, an amazing basal metabolism. The Babe, for many years, has eaten about ten meals a day. And his radiant heat is so intense that he cannot wear even the lightest underwear on the coldest day of winter.
>
> Had we the figures here on all these characteristics, we should find that Babe Ruth, far from being a 'man in a million,' is at least one man in fifty or sixty million.

For the layman this book probably has much more practical value than the "Sweet babble of the success cult." The author develops from a new angle the good old maxim "If at first you don't succeed, try, try again."

SOME BIOLOGICAL ASPECTS OF WAR.
By Harrison R. Hunt *Galton Publishing Co.*
$2.00 6 x 9; 118 *New York*

An attempt to investigate some of the effects of war on the genetic constitution of the population of the United States. The bulk of the study consists of a comparison of enlistment and death rates of Harvard College graduates, with similar rates for the country as a whole. It is shown that both enlistment and mortality rates were higher for the Harvard graduates, a result which the author regards as biologically unfortunate. The value of the study is reduced by a lack of clarity in exposition.

ERGEBNISSE DER SPORTÄRZTLICHEN UNTERSUCHUNGEN BEI DEN IX. OLYMPISCHEN SPIELEN IN AMSTERDAM 1928.
Papers by A. Bethe and E. Fischer; C. Bramwell and R. Ellis; M. and H. Bürger and P. F. Petersen; F. Deutsch; J. Dybowska and W. Dybowski; A. Fessard and H. Laugier; F. Heiss; H. Herxheimer; S. Hoogerwerf; O. Huntemüller; W. Kohlrausch; R. E. Mark; P. Schenk and K. Craemer; J. Snapper and A. Grünbaum; W. Thörner. Edited by F. J. J. Buytendijk. *Julius Springer*
6½ x 9½; vii + 230 (paper)
12 marks *Berlin*

An interesting collection of papers, representing observations taken on participants in the Amsterdam Olympics. It is unfortunate that refusal to cooperate on the part of the officials of some of the larger nations (in particular the United States and England) reduces very considerably the number of noteworthy performers. For example, in Bramwell and Ellis' paper

on clinical observations, 202 athletes were examined; of these one man won the 100 and 200 metres; and the first and second place winners in the weight lifting were also examined. It is to be hoped that the officials in charge of the 1932 Olympics will assist in arranging further studies of this nature.

THE HISTORY OF THE AMERICAN PEOPLE.

By John H. Latané *Allyn and Bacon*

$2.00 5½ x 7⅞; xviii + 827 *New York*

This book is more than a revision of the author's *History of the United States*. While the narratives of wars have been reduced to a mere outline of the more important campaigns, and political history has been simplified by the omission of many details, chapters have been added dealing with social, economic, industrial, and artistic development. As a native of a border state Dr. Latané is able to give a more unbiassed interpretation of the difficulties between the North and the South than many earlier text-book writers.

NOTES ON THE NATIVES OF CERTAIN VILLAGES OF THE MANDATED TERRITORY OF NEW GUINEA. *Visited During the Voyages of the Government Steam Yacht "Franklin," January-March, 1925. Anthropological Report No. 1.*

NOTES ON THE NATIVES OF E MIRA AND ST. MATTHIAS. *Anthropological Report No. 2.*

CERTAIN NATIVES IN SOUTH NEW BRITAIN AND DAMPIER STRAITS. *Anthropological Report No. 3.*

By E. W. Pearson Chinnery

Commonwealth Offices, Australia House

Free *London*

6 x 9½; Nos. 1 and 2 bound together, 238 (paper)
No. 3, 102 (paper)

In these reports the Government Anthropologist gives a fairly detailed account of the natives of the island of E Mira, together with miscellaneous notes on natives of the former German New Guinea, New Britain, and other adjacent islands. In most of the villages visited the number of children per marriage was small. The volumes constitute first rate contributions to the vital statistics of primitive races.

PRENATAL CARE. *United States Department of Labor. Children's Bureau Publication No. 4.*

U. S. Government Printing Office

10 cents *Washington*

5¾ x 9; v + 71 (paper)

This excellent guide is not intended to make the expectant mother independent of the physician. Rather it has been prepared for those who are unable to consult a physician frequently and as a supplement to the doctor's instructions. Written briefly and simply, it contains the essential information which the pregnant woman should know. Included in the bulletin is a list of selected books of interest to mothers, a glossary and an index.

CHILDREN WHO RUN ON ALL FOURS *And Other Animal-like Behaviors in the Human Child.*

By Aleš Hrdlička

Whittlesey House (McGraw-Hill Book Co., Inc.)

$5.00 6 x 9; xx + 418 *New York*

This book is a report on 387 infants who ran on hands and feet instead of creeping on hands and knees. The children in whom this and related animal-like behaviors occur are mostly strong and healthy both physically and mentally. Dr. Hrdlička concludes that "just as the human child before birth recapitulates, more or less, various phases of its physical ancestry, so the child after birth recapitu-

lates and uses for a time various phases of its prehuman ancestral behavior."

KONSTITUTIONSTYPEN DER KINDER
By W. S. Krasusky *S. Karger*
4.20 marks *Berlin*
7 x 10; vi + 62 (paper)

In the development of children there are periods in which they grow more rapidly in height, alternating with periods of lateral growth. With these cycles of physical development are associated changes in temperament. Can we discern, underlying these cycles, a constant substratum of habitus? Is the future pyknic distinguishable throughout his development from the future leptosome? Dr. Krasusky thinks not, although the complexity of the problem prevents any definite yes or no.

OUR CITY—NEW YORK. *A Book on City Government.*
By the High School Students of New York City. Supervised by Frank A. Rexford
Allyn and Bacon
$1.20 5 x 7½; xx + 344 *New York*

A book on city government prepared by high school students in the New York public schools under the guidance and advice of the teachers. It is a second edition, entirely rewritten, with new illustrations, and is designed for use by the pupils in their study of New York City, its government, finances, education, health regulations, etc. The illustrations are numerous. There is an index.

AN INTRODUCTION TO PHYSICAL ANTHROPOLOGY.
By E. P. Stibbe *Longmans, Green and Co.*
$5.00 5⅜ x 8⅜; vii + 199 *New York*

A textbook for beginners, dealing with the technical knowledge necessary as a foundation for work in physical anthropology. The subject is dealt with from three viewpoints: (1) Zoological, (2) Paleontological, and (3) Ethnological. Three chapters deal with practical applications, and exercises for the student. There is a glossary.

LEITFADEN DER ANTHROPOLOGIE
By K. Saller *Julius Springer*
24 marks (paper) *Berlin*
25.80 marks (cloth)
6¾ x 10; ii + 284

This excellent introduction to physical anthropology is written by a pupil of Martin. There are a brief bibliography and an index.

ZOOLOGY

A HISTORY OF APPLIED ENTOMOLOGY (*Somewhat Anecdotal*)
By L. O. Howard *Smithsonian Institution*
$2.25 *Washington*
6½ x 9½; viii + 564 (paper)

The distinguished author of this delightful volume of somewhat rambling entomological reminiscences deserves well of his countrymen and of science generally. For it is a literal fact that he has done more than any other person who ever lived, first, to arouse public interest to a realization that insects are among the most formidable and menacing enemies to the continuance of human civilization, and, second, to devise and organize effective methods of defense against this menace. Doctor Howard has not only lived through the extraordinary rise of economic entomology to its present recognized importance among the agencies of human welfare. He has, to a remarkable degree, made it. Out of the wealth of contacts and intimate knowledge of persons and events which

his modest and self-effacing career as a public servant has somewhat automatically and necessarily entailed, he has accumulated a vast store of what current slang would call the "entomological dirt." Full of years and honors he has, quite apparently, had a lot of fun writing a book about it all. THE QUARTERLY REVIEW OF BIOLOGY ventures, in the name of all biologists, publicly to thank him for it.

The arrangement of the material is primarily geographical. Beginning with North America and going right around the world we are shown, in more or less detail according to circumstances, the history and present status of applied entomology in each country, with plenty of anecdotes along the way. Part VII deals with medical entomology, and with the use of predatory and parasitic insects as means of control. This latter field is one in which Doctor Howard has long been recognized as the outstanding leader. The volume ends with five half-tone plates of portraits of entomologists, and an index.

The book is a notable contribution to the history of biology.

DEMONS OF THE DUST. *A Study in Insect Behavior*
By William M. Wheeler
W. W. Norton and Co., Inc.
$5.00 6 x 9; xviii + 378 *New York*

In this book Professor Wheeler deals with two groups of insects belonging to widely different orders but with remarkably convergent behavior. The neuropteran ant-lions and the dipteran worm-lions in their larval stage capture their prey by excavating funnels in the sand, at the bottom of which they lie in wait. The book treats the taxonomy, distribution, anatomy and life history of the two groups, much of the material being derived from the author's own researches. The behavior of the larvae, he concludes, can not be analysed into simple or chain reflexes but must be considered "as a configuration, or 'Gestalt,' involving not only the insect but its specific environment as well." In conclusion he reviews the various predatory organisms that ambush instead of actively seeking their prey. These he dubs *lochētic*. Degeer's *Report on the worm-lion* and Réaumur's *History of the worm-lion fly* are given as appendices. There are also a bibliography of 26 pages and an index.

In his preface Professor Wheeler confesses his doubt whether he has not "crashed between two stools in attempting to interest both the entomologist and the general reader." No doubt the latter will skip much of the taxonomic and anatomic sections, but he will have only his own faint heart to blame if he allows these to scare him off from the fascinating historical and behavioristic sections. Altogether this is a great book, well worthy of its author.

THOMAS SAY. *Early American Naturalist.*
By Harry B. Weiss and Grace M. Ziegler
Charles C. Thomas
$5.00 postpaid *Springfield, Ill.*
6 x 9¼; xiv + 260

This is a meticulously thorough and scholarly account of the life of an important figure in the history of biology in America. In fact Dr. L. O. Howard, in his Foreword says that Thomas Say ranks "as the most eminent of the early American taxonomic zoologists." Born in Philadelphia of Quaker stock Say started out to keep a drug store, but his love of natural history and his indifference to wealth combined to lead him quickly into the career of professional naturalist, from which he never deviated. His solid fame

rests most securely upon his entomological work.

The authors deserve great praise, not only for the thoroughness of the research which has gone into their work, but for the breadth of viewpoint with which the work was planned. We are given a comprehensive picture of Say's life *in its setting*, something unfortunately lacking in many biographies of scientific men.

RECENT ADVANCES IN ENTOMOLOGY.
By A. D. Imms
P. Blakiston's Son and Co., Inc.
$3.50 net *Philadelphia*
5⅛ x 8; viii + 374

This book "attempts to review and discuss certain aspects of the subject along which recent advances have been fertile in new facts and ideas." Chapter headings are as follows: Some aspects of morphology (two chapters); Metamorphosis; Palaeontology; The sense organs and reflex behaviour (two chapters); The fundamental aspect of coloration; Some aspects of ecology (two chapters); The practical application of ecology (two chapters); Parasitism (two chapters); Biological control (two chapters).

The book contains illustrations, tables, and diagrams. Literature lists are frequently appended to the chapters and there are author and general indices. Advanced students of entomology and investigators in general biological problems will find this book of much interest.

LA PARTHÉNOGENÈSE.
By A. Vandel *G. Doin et Cie*
32 francs 4½ x 6⅞; xix + 412 *Paris*
(paper)

A useful treatise on parthenogenesis, primarily concerned with its natural occurrence among animals. The successive chapters cover: Discovery and interpretation, definition and extent, facultative parthenogenesis, cyclic parthenogenesis, paedogenesis, accidental parthenogenesis, parthenogenesis in nematodes, geographic parthenogenesis, the cytology of natural parthenogenesis, parthenogenesis in plants, the relations of experimental parthenogenesis to natural, parthenogenesis and sex, and general conclusions. The bibliography covers over seven hundred titles; there is both an author and a subject index.

HANDBOOK OF PROTOZOOLOGY
By Richard R. Kudo *Charles C. Thomas*
$5.50 *Springfield, Ill.*
5½ x 8¾; x + 451

This is a handbook of interesting information on the common and representative genera of all the groups of both free-living and parasitic Protozoa. The text is in two parts. Part I consists of three chapters on morphology, physiology and reproduction of Protozoa. In the second part are thirty chapters dealing with the taxonomy, biology and development of common Protozoa. The author has gathered together much material which until now has been widely scattered and unavailable to the average student. The work includes keys, numerous excellent illustrations, reference lists for each chapter, and a detailed index.

A useful handbook for teachers, field workers, physicians, veterinarians and public health workers.

THE FUR SEAL OF THE CALIFORNIA ISLANDS *with New Descriptive and Historical Matter. Zoologica, Volume IX. Number 12.*
By Charles H. Townsend
New York Zoological Society
Zoological Park, New York City
6¼ x 9¼; 15 (paper)

This paper is an account of a species that was long supposed to be extinct. Weather-worn skulls found on Guadalupe Island, Lower California, in 1892 by the author showed it to be an undescribed species. It was named *Arctocephalus townsendi* by Merriam.

The species reappeared at Guadalupe in 1928 and two adult males were sent to the Zoological Garden at San Diego where they were photographed. When they died a skin and skeleton were presented to Dr. Townsend, who here describes skin and perfect skull from the first animal available for the purpose.

The paper contains new matter relative to its slaughter in the nineteenth century. It is illustrated with a colored plate and several photographs.

DIE TIERWELT DER NORD- UND OSTSEE. *Lieferung XVIII.*
Edited by G. Grimpe and E. Wagler
Akademische Verlagsgesellschaft m.b.H.
13.50 marks *Leipzig*
6 x 8½; 147 (paper)

DIE TIERWELT DER NORD- UND OSTSEE. *Lieferung XIX.*
Edited by G. Grimpe and E. Wagler
Akademische Verlagsgesellschaft m.b.H.
12.80 marks *Leipzig*
6 x 8½; 136 (paper)

These two parts of this useful survey of the fauna of the North and Baltic seas, previous numbers of which have been noted in these columns, deal with the following groups: Phyllopoda, by W. Rammner; Isopoda genuina, and Anisopoda, by H. F. Nierstrasz and J. H. Schuurmans Stekhoven, Jr.; parasitic Peridinea, by E. Reichenow; Kamptozoa, by C. I. Cori; and thalassobiontic and thalassophile Diptera Brachycera, by O. Karl.

HANDBUCH DER BIOLOGISCHEN ARBEITSMETHODEN. *Lieferung 346.* Containing following articles: *Materialbeschaffung, Lebendbeobachtung und Haltung von Tardigraden*, by Ernst Marcus; *Sammeln, Züchtung und Untersuchung von Zecken*, and *Sammeln, Züchtung und Untersuchung der Flöhe*, by E. N. Pawlowsky; *Methodik der Erforschung der subterranen Fauna*, by P. A. Chappuis.
Urban und Schwarzenberg
13 marks 7 x 10; 226 (paper) *Berlin*

In this number of the Abderhalden *Handbuch* the most interesting articles to the general biologist are those on the tardigrades and the subterranean fauna; those on the culture of ticks and fleas will be useful to the parasitologist.

ENTWICKLUNGSPHYSIOLOGIE DER TIERE. *Wissenschaftliche Forschungsberichte Band XXII.*
By Paul Weiss *Theodor Steinkopff*
11 marks (paper) *Dresden and Leipzig*
12.20 marks (bound)
6 x 8¾; xi + 138

This excellent little book presents the physiology of development with special reference to the advances of the last dozen years.

THE FAUNA OF BRITISH INDIA, INCLUDING CEYLON AND BURMA. *Cestoda. Vol. II*
By T. Southwell *Taylor and Francis*
15 shillings 6 x 9; ix + 262 *London*

The second volume of this monograph is devoted to the Tænioidea. It also contains classified lists of Indian cestodes and their hosts and an index.

THE WATER EXCHANGES OF LIVING CELLS. *I. The Normal Permeability of the Eggs of Some Marine Invertebrates. University of California Publications in Zoology, Vol. 36, No. 7.*
By James L. Leitch
University of California Press
25 cents 7⅛ x 10¾; 14 (paper) *Berkeley*

NOTES ON THE GENUS ENDOSPHAERA ENGELMANN AND ON ITS OCCASIONAL HOST OPISTHONECTA HENNEGUYI FAURÉ-FREMIET. *University of California Publications in Zoology, Vol. 36, No. 5*

By James E. Lynch and Alden E. Noble.

University of California Press

25 cents $7\frac{1}{8}$ x $10\frac{3}{4}$; 18 (paper) *Berkeley*

A STUDY OF THE SPECIES OF EIMERIA OCCURRING IN SWINE. *University of California Publications in Zoology, Vol. 36, No. 6.*

By Dora P. Henry

University of California Press

25 cents $7\frac{1}{8}$ x $10\frac{3}{4}$; 12 (paper) *Berkeley*

THE MORPHOLOGY AND LIFE-CYCLE OF OXYMONAS DIMORPHA SP. NOV., FROM NEOTERMES SIMPLICICORNIS (BANKS). *University of California Publications in Zoology, Volume 36, No. 2.*

By Frank H. Connell

25 cents 7 x $10\frac{3}{4}$; 16 + 3 plates (paper)

HYPERMASTIGOTE FLAGELLATES FROM THE TERMITE RETICULITERMES: TORQUENYMPHA OCTOPLUS GEN. NOV., SP. NOV., AND TWO NEW SPECIES OF MICROJOENIA. *University of California Publications in Zoology, Volume 36, No. 3.*

By Virginius E. Brown

University of California Press

25 cents *Berkeley*

7 x $10\frac{3}{4}$; 12 + 5 plates (paper)

COPEIA. *A Journal of Cold-Blooded Vertebrates. Established in 1913. The David Starr Jordan Anniversary Number. 1930, No. 4.*

American Society of Ichthyologists and Herpetologists

50 cents *Ann Arbor, Michigan*

Subscription price of journal (quarterly) $2.00 per annum

$6\frac{3}{4}$ x $9\frac{3}{4}$; 76

BOTANY

SIZE AND FORM IN PLANTS. *With Special Reference to the Primary Conducting Tracts*

By F. O. Bower *The Macmillan Co.*

$4.50 $5\frac{3}{4}$ x $8\frac{1}{2}$; xiv + 232 *New York*

No better conception of this important book can be given than by quoting certain passages from the author's preface. He says

"In approaching a problem so extended as that of the relation between Size and Form in Plants at large, it is desirable in the first instance to select some limited field of observation: preferably it should be one in which those difficulties, which increasing size necessarily entails, have not been so successfully surmounted by adaptation as they have been in some of the Highest Plants. The features compared should also be readily open to measurement, whether the material be in the living or in the fossil state. The conducting tracts, and in particular the wood which is as a rule well preserved in fossils, afford the best opportunity for comparative treatment." "Under the name 'Size-Factor' is connoted that influence which tends to secure by modification of Form a due levelling up of the proportion of surface to bulk as the Size increases. Whatever that influence may be, the measurements of growing plants that depend on primary development show consistently its effect in modifying Form, external or internal. It may be described as a Morphoplastic Factor. The evidence that it does act in moulding the tissues is widespread, and its incidence is insistent and unavoidable. The development of this conception and a detailed record of the results of its action form the substance of this book." His aim has been to follow a middle course between the physiologists who study function, and the morphologists who study form. ". . . certain structural facts have been stated in their relation to function: in fact they have been treated organographically. For this purpose a very considerable field of observation has been advanced, with approximate

rather than absolute measurements. Certain conclusions as to Size and Form have followed, and they are set down here in their biological aspect. It is the hope of the author that by venturing thus upon a comprehensive statement of fact and inference from the side of Morphology, the problems of the physiologist may present themselves with an added interest and point, and that the result may be a better common understanding.

The text of the book is devoted to a study of the Pteridophyta, both living and fossil forms. There are also sections on the shoots of seed plants, and on roots and a chapter on the plasticity of form and structure in relation to size. The work includes tables of measurements and ratios, 72 figures, mostly cross sections of stems and roots, and an index.

ELEMENTS OF PLANT SCIENCE
By Charles J. Chamberlain
McGraw-Hill Book Co., Inc.
$1.90 5⅜ x 8; xii + 394 *New York*

This excellent introduction to the study of plants will be extremely useful in schools giving a beginning course in botany. It is so arranged that it can be used in places where microscopes are not available and only one semester is given to plant study. It provides, however, for a year's work and covers, in outline, a considerable part of the subject matter of botany. The many carefully selected illustrations and the section on laboratory methods add greatly to the value of the book. There is an index.

RUBBER. *An Economic and Statistical Study.*
By José Carlos deM. Soares
Richard R. Smith, Inc.
$3.00 5½ x 9; xii + 93 *New York*

An exhaustive survey of the history of the decline of the rubber industry in Brazil, the causes of the decline, and the growth of competition in foreign countries. The author also incorporates in the book plans for the future reorganization of the industry which should lead to the rehabilitation of one of Brazil's chief sources of wealth. Much statistical material is given on world production and consumption of rubber, profits and dividends of rubber companies, duties on rubber, etc. There is no index.

PLANT ECOLOGY. *Second Edition, Thoroughly Revised*
By W. B. McDougall *Lea and Febiger*
$3.00 net 5¼ x 7¾; 338 *Philadelphia*

OBSERVATIONS SUR LA BIOLOGIE DE QUELQUES CHAMPIGNONS.
By Roger Martin
40 francs net
6½ x 10; 115 (paper)

ÉTUDE COMPARATIVE DE BACILLUS MESENTERICUS FUSCUS FLÜGGE ET DE BACILLUS MESENTERICUS NIGER LUNT. *Thèse présentée et soutenue publiquement le Mercredi 2 Juillet 1930 à la Faculté de Pharmacie de Nancy pour obtenir le titre de Docteur de l'Université de Nancy (Mention Pharmacie)*
By Pierre Thomas
40 francs net
6½ x 10; 138 (paper)

TRAVAUX DU LABORATOIRE DE MICROBIOLOGIE DE LA FACULTÉ DE PHARMACIE DE NANCY.
By MM. Lasseur and Vernier
6½ x 10; 189 + 7 plates

CONTRIBUTION A L'ÉTUDE DE LA COLORATION DE GRAM. *Étude Critique de la Coloration de Gram. Essai sur la Modification de Gottstein. Essai de Stabilisation de la Solution Colorante de Violet de Gentiane Phéniqué.*
By Georges Coudray
40 francs net
6½ x 10; xii + 112 (paper)

CONTRIBUTION A L'ÉTUDE DE LA PRÉCIPITATION ET DE L'AGGLUTINATION SÉRIQUES DES CHAMPIGNONS.
By Paul Martin
60 francs net
6½ x 10; 211 + 5 plates (paper)

CONFÉRENCES FAITES AU LABORATOIRE DE MICROBIOLOGIE DE LA FACULTÉ DE PHARMACIE DE NANCY.
By G. Darmois, M. Dufour, A. Travers, G. Vavon, Pierret, R. Collin, Ph. Guinier, Ed. Gain, L. Nègre, Patriat and P. Vitu.
Laboratoire de Microbiologie de la Faculté de Pharmacie de Nancy
60 francs net *Nancy*
6½ x 10; 271 (paper)

LES VARIATIONS LAURENTIENNES DU POPULUS TREMULOIDES ET DU P. GRANDIDENTATA. *Contributions du Laboratoire de Botanique de l'Université de Montréal.—No. 16.*
By Frère Marie-Victorin
50 cents 6 x 9; 16 (paper)

LE GENRE RORIPPA DANS LE QUÉBEC. *Contributions du Laboratoire de Botanique de l'Université de Montréal.—No. 17.*
By Frère Marie-Victorin
Laboratoire de Botanique Université de Montréal
50 cents *Montreal*
6 x 9; 17 (paper)

L'ANACHARIS CANADENSIS. *Histoire et solution d'un imbroglio taxonomique. Contributions du Laboratoire de Botanique de l'Université de Montréal, No. 18.*
By Frère Marie-Victorin
Université de Montréal
75 cents *Montreal, Can.*
6 x 9; 43 (paper)

REPORT ON THE PREPARATION OF FRUIT FOR MARKET, (*Part II: Gooseberries, Currants, Cherries, Raspberries, Loganberries, Tomatoes, Cucumbers and Grapes*). *Economic Series No. 24.*
Ministry of Agriculture and Fisheries
H. M. Stationery Office
London
British Library of Information
551 Fifth Ave., New York
6 d. net 6 x 9½; 98 (paper)

MORPHOLOGY

THE ORIGIN OF THE HUMAN SKELETON. *An Introduction to Human Osteology*
By R. Broom *H. F. and G. Witherby*
10s. 6d. net 5½ x 8¾; 164 *London*

For thirty odd years Dr. Broom has been studying fossil forms of South African mammal-like reptiles in an endeavor to find the ancestor of the mammals. His investigations have led him to believe that he has been successful in tracing the origin of mammals and in solving the problem of the origin of lizards and crocodiles. Important facts have also appeared bearing on the evolution of the dinosaurs and birds. Pending the completion of a monograph on his researches he has issued this book which, in briefer form, presents the main results of palaeontology bearing upon the structure of the mammals. While designed for the student of anatomy, teachers of biology will find it full of interesting material for the general student. It is a comparative anatomy of the vertebrate skeleton from the fishes to the amphibians and primitive reptiles, the mammal-like reptiles and the mammals. The work includes many well chosen illustrations, a diagram of the evolution of the different forms, a bibliography and an index.

PRINCIPLES OF FUNCTIONAL ANATOMY OF THE RABBIT
By Edward D. Crabb *P. Blakiston's Son and Co., Inc.*
$1.50 5½ x 8¼; ix + 137 *Philadelphia*

Teachers of general biology and premedical students, and of students majoring in physical education, will find this an excellent guide for a course in elementary anatomy. Emphasis is put on the functional rather than on the purely descriptive point of view. The entire outline may be covered in something like one hundred hours of laboratory work. In two preliminary sections the author describes (a) the necessary laboratory equipment and material and (b) the elementary tissues. The book is sufficiently illustrated and contains an index.

L'ŒUF *et les Facteurs de l'Ontogénèse.*
By A. Brachet *Gaston Doin et Cie*
32 francs 4½ x 7; 438 (paper) *Paris*

In this second edition of Professor Brachet's book on causal embryology, a subject which owes so much to his researches, the chapters on maturation, the inertia of the unfertilized egg, fecundation, and parthenogenesis have been rewritten, and a new chapter on organizing centers and germinal localizations has been added.

PHYSIOLOGY AND PATHOLOGY

LES PHÉNOMÈNES DE CHOC DANS L'URTICAIRE. (*Étude Clinique et Thérapeutique*).
By Pasteur Vallery-Radot and Lucien Rouquès. *Masson et Cie*
35 francs 6 x 9¼; 232 (paper) *Paris*

Anyone who has ever treated many patients with urticaria will welcome information on the subject. Everyone assumes that urticaria is due to eating some food to which the body is sensitive; the trouble is to find the food. Sometimes the hives continue to appear even when the patient is desperate enough to go for a week without eating. Actually, it is now coming to be recognized that there are other causes for urticaria such as nervous shock, muscular effort, and exposures to heat and cold. Some persons get urticaria when they lose their temper.

In this book the authors prefer to use the term "Colloidoclasic crisis," instead of the old term "hemoclasic crisis," because the phenomenon concerned is not limited to changes in the blood. There are at least four types of urticaria; the first is due perhaps to a fairly simple anaphylaxis. The second is due to reactions more complicated than those of simple anaphylaxis as the changes in the body are brought about slowly and insidiously and as a result of repeated contacts with antigen. In the third group the first contact of the patient with the antigen seems to be enough to produce the reaction, and one must assume that the subject possesses from the start an idiosyncrasy, probably hereditary in nature. In the fourth group the urticaria is produced without the intervention of any antigen coming from outside the body.

The book is interesting and readable. Many points are illustrated with brief case histories; but some readers will doubtless disagree with the interpretations made. The various methods of treatment now being used in France are described and conservatively appraised. There are a number of interesting charts showing the ways in which the leucocyte count changes from hour to hour during an attack of urticaria.

LE SYSTÈME GLANDULAIRE ET VUES NOUVELLES EN MÉDECINE.
By Francesco Cavazzi *Gaston Doin et Cie*
14 francs 7 x 10; 45 (paper) *Paris*

ON PEUT RAJEUNIR. *La fonction énergétique de la sécrétion interne testiculaire et les injections sous-cutanées de produits de sécrétion interne testiculaire pour redonner les énergies organiques aux hommes affaiblis par l'âge et par le travail et pour prolonger leur vie. Rapport de faits expérimentaux.*

By Francesco Cavazzi *Gaston Doin et Cie*

25 francs *Paris*

7 x 10; 68 + 21 portraits (paper)

These two treatises go together. The first is supposed to furnish the rational foundation for the second, which sets forth the alleged consequences of the supposedly practical application of what the author believes to be physiological principles, with that naïve optimism which is such a delightful characteristic of the Latin races when their digestions are working well. The general idea is that if one injects subcutaneously into old and enfeebled men "*de produits de sécrétion interne testiculaire,*" the old boys become once more parabolic, hydraulically speaking, and in other ways which Reginald, the Office Boy, says we musn't mention in a family magazine, get back on the up and up pathway. The second volume shows serial photographs of some of the patients, taken before, during, and after. In their stern and purposeful lugubriosity they are reminiscent of the Smith Bros., Trade and Mark. The trouble about it all is, first, that we are nowhere told precisely what it is that is injected, how it is obtained, or what the dosage is; and, second, that the evidence of rejuvenation which is presented would not convince even a beginning biology student in Bryan University, Dayton, Tennessee.

HYPERTENSION

By Leslie T. Gager

The Williams and Wilkins Co.

$3.00 6 x 9; xiii + 158 *Baltimore*

This review of the literature of hypertension will be found very useful as a reference work. Its point of view is primarily clinical. Furthermore the author is soundly conservative. The truth is, and it is an odd fact considering the enormous amount of effort which has been put upon its study, that while a great deal is known *about* hypertension as a phenomenon, extremely little is known of its essence, its causation. In the meantime, as Doctor Gager says (p. 88): "The future of patients with arterial hypertension, as a group, falls within limits so definite in respect of longevity and mode of death as to have almost the force of natural law. The prognostic significance of high blood pressure has been firmly established by the data of life insurance medicine."

There is a bibliography of 505 titles and detailed author and subject indexes.

THE CLINICAL INTERPRETATION OF BLOOD EXAMINATIONS

By Robert A. Kilduffe *Lea and Febiger*

$6.50 net $5\frac{3}{4}$ x $9\frac{1}{4}$; 629 *Philadelphia*

This extensive survey of blood tests and their clinical indications, applications and significance will be of value to physicians. The author has incorporated in his book two treatises which he issued some years ago on (1) *The clinical interpretation of the Wasserman reaction* and (2) *The clinical interpretation of blood chemistry*. Both of these have been greatly amplified, revised and extended to cover the field of laboratory examinations pertaining to the blood. The important work of other investigators has been reviewed and the results presented for the benefit of those who are unable to go to the original sources. Not only those methods have been included whose value is definitely understood but also those methods whose value was presumable, though very questionable and in some cases even definitely disproved. The work includes

numerous figures and tables, literature references and a detailed index.

LA THÉRAPEUTIQUE MODERNE
By Gabriel Florence *Armand Colin*
10 francs 50 4⅜ x 6¾; 202 (paper) *Paris*

This excellent little book is not a treatise on therapeutics, but an explanation for the general reader of some of its fundamental principles. In the first part are treated the biological problems of the intracellular penetration of therapeutic substances and their transformation by the organism. In the second part examples of the synthesis of new therapeutic agents by the chemist are given. The third part deals with immunity and anaphylaxis; the fourth, with vitamines and hormones. A résumé of the resolutions of the international conferences for the biological standardization of drugs and a bibliography conclude the book. There is no index.

HYPERSENSIBILITÉS SPÉCIFIQUES DANS LES AFFECTIONS CUTANÉES. *Anaphylaxie. Idiosyncrasie.*
By Pasteur Vallery-Radot et Mlle. V. Heimann *Masson et Cie*
25 francs 6 x 9⅜; 146 (paper) *Paris*

This little book gives a clear exposition of the French views on the subject of cutaneous hypersensitiveness. The authors discuss different types of urticaria, edema and eczema, and describe the various methods used in attempting desensitization. They take up in detail also the various methods of diagnosis. The style is lucid and the book is readable. Many of the points made are illustrated by case histories. There are good indexes, and the bibliography is adequate, although there is a preponderance of references to French writers. It is a worth while addition to books on this subject.

RIDERS OF THE PLAGUES. *The Story of the Conquest of Disease.*
By James A. Tobey *Charles Scribner's Sons*
$3.50 5¾ x 8½; xv + 348 *New York*

De Kruif's *Microbe Hunters* naturally comes to mind when reading this book. It is a pity, perhaps, for de Kruif's book was an exception to all rules. The present volume is entertaining popular scientific history; de Kruif's came close to genius. Tobey covers much more ground; and he is particularly interested in public health work. His book will furnish good entertainment for an evening's reading.

CHRONIC ARTHRITIS AND RHEUMATOID AFFECTIONS *with Recovery Record By Bernard L. Wyatt, with the Collaboration of Louis I. Dublin.*
William Wood and Co.
$2.50 5½ x 8¼; ix + 166 *New York*

Although arthritis and the rheumatic affections rank low as causes of death, they are responsible for a vast amount of suffering and economic loss. This book on their treatment emphasizes the importance of early diagnosis and the fact that many of the sufferers can be greatly improved in condition or even cured.

LE CHOC ANAPHYLACTIQUE ET LE PRINCIPE DE LA DÉSENSIBILISATION
By A. Besredka *Masson et Cie*
30 francs 5½ x 9; 276 (paper) *Paris*

In this monograph Professor Besredka tells what is known of the curious phenomenon of anaphylaxis. Of especial interest is his account of his experiments on antianaphylactic vaccination.

MÉTABOLISME ET FONCTIONS DES CELLULES. *Esquisse d'une Physiologie des Réactions Productrices d'Énergie dans la Cellule Vivante.*
By L. Genevois *Masson et Cie*
26 francs *Paris*
6½ x 9⅝; vii + 118 (paper)

This is a review, for French readers, of the researches on cell metabolism of Meyerhof and Warburg and their students and followers. It is very well done. There is an extensive bibliography, but no index.

ÜBER DAS PROBLEM DER BÖSARTIGEN GESCHWÜLSTE. *Eine experimentelle und theoretische Untersuchung. Zweiter, Abschliessender Band.*
By Lothar Heidenhain *Julius Springer*
42 marks (paper) *Berlin*
47.60 marks (bound)
10 x 13; vi + 207

The first volume of this admirable study of cancer was reviewed in the QUARTERLY REVIEW OF BIOLOGY for March, 1929. Further work confirms the author in his conclusion that the causative agent of cancer is a virus. The difference between the percentage of malignant tumors in inoculated mice and in controls is statistically significant.

DAS GEHEN. *Und seine Veraenderung durch verschiedene Umstaende. Auf Grund experimenteller Untersuchungen.*
By Adolf Basler
Verlag der Sun Yatsen-Universitaet Canton
(European agent: Gustav Fock.
18 marks 7 x 10½; xi + 272 *Leipzig)*

A careful study of the kinematics and dynamics of walking, based in large part on the author's own experiments. There is an index.

ANNALS OF THE PICKETT-THOMSON RESEARCH LABORATORY. *Vol. VI. The Pathogenic Streptococci. The Rôle of the Streptococci in Scarlet Fever.*
The Williams and Wilkins Co.
$10.00 *Baltimore*
8½ x 11; xiii + 470 (paper)
Bailliere, Tindall and Cox
£2, 2s. net *London*

BIOCHEMISTRY

LE PH ET SA MESURE
By M. Huybrechts *Masson et Cie*
15 francs 4¾ x 7½; 227 (paper) *Paris*

This clearly written little book will be useful to those who want to know what hydrogen ion concentration means, and how it is measured, but who lack the knowledge of physical chemistry necessary to understand the more technical treatises on the subject.

DONNÉES NUMÉRIQUES DE BIOLOGIE.
BIOLOGY (*Numerical Data*). *Extracted from Volume VII of Annual Tables of Constants and Numerical Data (years 1925–1926).*
By E. F. Terroine and M.-M. Janot
Gauthier-Villars et Cie
60 francs (cloth)
55 francs (paper) *Paris*
8¾ x 10½; xx + 68

An extract from Vol. VII of the Annual Tables published under the auspices of the International Research Council and of the Union of Pure and Applied Chemistry, covering the literature of 1925–26. The data are chiefly biochemical.

HANDBUCH DER BIOLOGISCHEN ARBEITSMETHODEN. *Lieferung 342.* Con-

taining following articles: *Potentiometrische Mikrotitration*, by Günther Rienäcker; *Pufferung und Puffersysteme*, by Franz Leuthardt; *Registrierung der Wasserstoffionenkonzentration im strömenden Blut*, by Robert Brinkman; *Die Bestimmung von Gas- und Dampfdrucken*, by Hans Fischer and Otto Rebmann. *Urban und Schwarzenberg*
17 marks 7 x 10; 288 (paper) *Berlin*

This number of the Abderhalden *Handbuch* will be chiefly of interest to the biochemists and physiologists.

MIKROCHEMISCHES PRAKTIKUM. *Eine Anleitung zur Ausführung der wichtigsten mikrochemischen Handgriffe, Reaktionen und Bestimmungen mit Ausnahme der quantitativen organischen Mikroanalyse. Zweite Auflage.*
By Friedrich Emich. (Mit einem Abschnitt über Tüpfelanalyse by Fritz Feigl.) *J. F. Bergmann*
12.80 marks (paper) *München*
6 x 9¼; xii + 157 (paper)

A revised edition of a useful microchemical *vade mecum.*

PROXIMATE COMPOSITION OF FRESH VEGETABLES. *U. S. Department of Agriculture Circular No. 146.*
By Charlotte Chatfield and Georgian Adams *U. S. Government Printing Office*
5 cents 5¾ x 9; 24 (paper) *Washington*

SEX

SEX GLANDS FUNCTION AND THE HUMAN LIFE.
By C. Leventis *C. Leventis*
$2.00 *911 Kresge Bldg., Detroit*
5¼ x 7¾; 132

This little book is well adapted to reading aloud in the biologist's home. We offer a few extracts:

Giving to all new born babies as a standard food, the cow's milk, and not their mother's milk, we will impress the glands in their function of all babies in a similar way. As a result all human beings will be of the same type of character, without individuality. They may be strong in their physical construction, but, in my opinion, they will be low in their mental power.

Grafting the gonads of the civilized human organism on the organism of chimpanzees or gorillas would be a profoundly interesting experiment. To me it is fraught with encouraging possibilities of success. There is little doubt that it would result in improving these wild organisms.

This could be probably accomplished in the following way:

The offsprings of chosen pairs of male and female gorillas would be grafted with human gonads very early in their lives before the reproductive function of the ape's gonads starts. During their lives they would receive injections of human serum. By treating their offspring in the same way for a few generations it might be possible to obtain a species nearer to the human race, if not quite resembling it. At least, the new species would be endowed with more human qualities than the gorilla. The intelligence of these animals could be developed by training and thus produce an educated and civilized species of animal which probably would form a missing link between the human race and the higher apes.

By such a procedure it is not impossible to impress the reproductive function of the gonads of the animals by the absorption and assimilation of the implanted human gonads and by the injection of the human serum. This might be followed by a spontaneous mutation into the gonads of that inferior animal organism, and thus help nature in its tendency toward evolution. In this event there would be produced a more accomplished and farther evolutionized living being, with developed reproductive elements for the preservation of its species.

Modern women, being free to gratify their autoerotic feeling by exposition of their body, do that in a rather scandalous social manner to the great harm of their other feelings and charms. If they endeavor to excuse this by saying that they do so in order to be more attractive to men, they are mistaken. On the contrary, they spoil that prestige of the hidden and occult upon the men. Arms and legs of women are not comparable to the different bottles of liquor exposed in the windows of shops before prohibition.

We passed them indifferently. Now that such bottles are mysteriously hidden their attractiveness is greatly magnified.

Women must abandon and forget most of their feminine sex impetus for a more respectful social life, otherwise fathers, brothers, sons, and school boys will not avoid evil suggestions and thoughts through the impressions arising from seeing the naked legs of their daughters, teachers, sisters and mothers. We have many such examples today.

HEALTH AND CONTINUAL YOUTH.
By Mary Marriott Radcliffe.
The Norman Remington Co.
$2.00 9 x 12; 19 *Baltimore*

This beautifully produced book maintains the odd thesis that the congress of the sexes is biologically harmful. In the actual words of the author

> These pages give evidence of the injury of sex to health, morale and duration of life, and the logical and ideal solution, with supporting evidence, that mankind shall overcome disease and death, and keep alive the clean, gay, vibrante [*sic*] spirit of youth—through steadily increasing and total sex abstinence, sunlight, rest, diet and other necessary hygiene.

We are unable to discover in the book any evidence which, in our opinion, is either valid or pertinent so far as concerns that part of the thesis pertaining to the relation of "sex abstinence" to "disease and death."

There is included a long table of figures, furnished chiefly by veterinarians, which gives estimates and opinions as to the extreme ages at death which may be attained by stallions, mares, geldings, oxen, and bulls. In our opinion the data in this table are so far at variance with the canons of sound statistical procedure, particularly relative to random sampling, as not to be worthy of any serious consideration whatever.

MARRIAGE. *Past, Present and Future. An Outline of the History and Development of Human Sexual Relationships.*
By Ralph de Pomerai
Richard R. Smith, Inc.
$4.00 net *New York*
$5\frac{3}{8}$ x $8\frac{1}{2}$; xvii + 370

A survey of the history, present conditions, and desirable reforms in that state which St. Paul described as better than burning. The author has produced a moderately interesting book, though we are not always convinced by his arguments. Why, however, does he describe the author of *Erewhon* as "Bishop" Butler?

EARLY THEORIES OF SEXUAL GENERATION.
By F. J. Cole *Oxford University Press*
$6.00 $5\frac{1}{2}$ x $8\frac{3}{4}$; x + 230 *New York*

This book is primarily concerned with the history of the Preformation Doctrine. The author has, on the whole, succeeded admirably in telling a clear and interesting story of what might appear a dull tangle of scientific speculation and error. The book is a valuable contribution to the history of science.

PHYSICIANS' MANUAL OF BIRTH CONTROL.
By Antoinette F. Konikow
Buchholz Publishing Co.
$4.00 6 x 9; xiii + 245 *New York*

A treatise for physicians on the technique of contraception, on the whole well done. There is a statistical section based on the author's clinical experience; it is, unfortunately, as inadequate as all others we have seen as evidence of the real effectiveness of the techniques involved.

BIOMETRY

NUMERICAL MATHEMATICAL ANALYSIS.
By James B. Scarborough *The Johns Hopkins Press*
$5.50 $6\frac{1}{8}$ x $9\frac{1}{2}$; xiv + 416 *Baltimore*

A useful treatise for anyone who has occasion to obtain numerical results from his mathematics. The treatment is considerably more detailed and elementary than that in Whittaker and Robinson. As a result, a number of topics treated in the latter are not found in the present volume. On the other hand, the beginning computer will probably find this a less difficult work to follow.

LEÇONS SUR LA THÉORIE MATHÉMATIQUE DE LA LUTTE POUR LA VIE.
By Vito Volterra *Gauthier-Villars et Cie*
60 francs *Paris*
$6\frac{1}{2}$ x 10; vi + 214 (paper)

It is hoped that a detailed review of this book will appear in an early number of THE QUARTERLY REVIEW OF BIOLOGY.

PSYCHOLOGY AND BEHAVIOR

ANIMAL DRIVE AND THE LEARNING PROCESS. *An Essay Toward Radical Empiricism. Vol. I. (With a supplementary essay on "This Material World," by Harold C. Brown).*
By Edwin B. Holt *Henry Holt and Co.*
$2.50 $5\frac{1}{4}$ x 8; x + 307 *New York*

This book is a presentation of psychology in purely physiological terms, based in large part on Bok's principle of the reflex circle. The first volume deals with the development of the simpler types of behavior, while the second will treat the higher psychic functions. With our present limited knowledge of neural physiology much of the account is necessarily hypothetical, but it is well worth while to show that psychological phenomena can be reasonably stated in terms of known types of physiological process, even though the proof or disproof of the details must be left to future experiment.

Dr. Holt has a pungent wit and is not afraid to speak out in meeting as is shown by the following and other passages:

> The sexual appetite is so hedged about by taboos, superstitions, and lies, that any true statement about it will meet with a thousand frenzied denials. So if I say that the sexual appetite, like all other appetites, is imperative and like the others does not brook indefinite delay, there will be loud cries of dissent, to the general purport that "pure thoughts, hard exercise, cold water and prayer" will divert the sexual appetite for a lifetime. To those in whom the sexual appetite arouses "impure thoughts" I make no doubt that cold water and prayer will prove beneficial. For indeed I suppose that the most, and perhaps the only, impure thought connected with sex is the thought to perpetuate the stereotyped lies about it. But if there is anybody who honestly imagines that this appetite ever has been or ever will be beguiled by any such precautions, he should find his attention instantly claimed by the attractive themes of sexual perversion and the neurotic disorders, and *why they happen*. He will also find it interesting and profitable to study the phenomena of "cultural" mendacity, and the "as if" hypocrisies. And yet even the Freudians, who ought to know better, follow the accepted superstitions with their theory of sexual "sublimation"—a colossal blunder—and the unctuous rubbish about "cultural" (*kulturelle*) aims. Of course, if by artificial, "educational" means this or any other appetitive restlessness *is* drafted off into motor channels other than those that appease the appetite, the individual is successfully wrecked.

CONDITIONS AND CONSEQUENCES OF HUMAN VARIABILITY.
By Raymond Dodge *Yale University Press*
$2.50 6 x 9; xi + 162 *New Haven*

The older generation of physicists were

accustomed to look down their noses at biology and especially at psychology. The study, we were told, of systems in which differences in the internal relations might make wide changes in the results obtained from successive trials with the same experimental set-up could scarcely be dignified with the name of science. Present-day physicists, having learned something of the caprices of the electron, are less snooty. Professor Dodge, however, glories in this infirmity of psychology and finds

> Variability to be not a mere accident impeding the development of a true science of behavior, experience, and personality, but rather an aspect of the observable facts that is quite as important as their commonly noticed relative stability. The conditions of variability reach into the elementary processes of neural action until one may say that a differential variability is the hypothesis that best fits the observable neuropsychological facts.
>
> The consequences of variability seem to reach into the very heart of mental reaction and mental development. One may say with some confidence that without variability there would be no mental development, either in the race or in the individual. The evidence suggests an even more fundamental relationship. One is tempted to substitute for the older materialistic doctrine, "Without phosphorus no thought," a newer psychophysiological generalization, "Without variability, no mind." But the variations must apparently be of definite and distinctive kinds, connected in a specific manner with systematizations of relative persistency.

THE MIND OF THE MURDERER.
By Harold Dearden

Sears Publishing Co., Inc.
$3.50 5½ x 8½; 288 *New York*

A tiresome piece of ostensibly "popular" scientific writing, of a sort calculated to make the judicious tearful. The technique is to take a murder case, as described in the newspapers or in earlier popular treatises on famous trials, and then try to concoct some sort of a psychological "explanation" of the murderer's supposed motives. The actual legal evidence of record is frequently strained, and sometimes even thrown overboard, to help in the development of the theory to fit a particular crime. Twenty cases are picked out for this so-called "psychological" treatment, going back as far as 1800. Those with a cultivated taste for the literature of crime will not be amused by this book. As compared with Roughead's delightful books in that field this is very poor pap indeed. There is no index, but it doesn't matter.

THE RELATIONS OF PSYCHOLOGY TO MEDICINE AND THE RECOGNITION AND TREATMENT OF COMMONER AFFECTIVE DISORDERS. *Porter Lectures Series I.*
By Lewellys F. Barker

University Extension Division, University of Kansas
75¢ (paper)
$1.00 (cloth) *Lawrence*
5¾ x 8½; 68

A series of three lectures delivered at the School of Medicine at the University of Kansas, under the Porter Foundation. The subjects of the lectures are as follows: (1) The Relations of Psychology to Medicine; (2) On Certain Disturbances of the Whole Personality with Especial Reference to the Commoner Affective-Conative Disorders; (3) Treatment of Personality Disorders, Especially of the Commoner Affective Disorders. The author, widely known for his eminence as a physician and teacher at the Johns Hopkins School of Medicine is well fitted to deal with these subjects. He emphasises the need of a knowledge of psychology and a thorough training in psychological methods of investigation for those engaged in medical work, the importance of being well acquainted with the criteria necessary for

the recognition of the disturbances of feeling emotions in the different psychoneuroses, and outlines a comprehensive plan of therapy.

Each section contains lengthy literature lists. There is no index.

THE GUIDANCE OF MENTAL GROWTH IN INFANT AND CHILD.
By Arnold Gesell *The Macmillan Co.*
$2.25 5½ x 8½; xi + 322 *New York*

The author is Director of the Yale Psycho-clinic and Professor of Child Hygiene in Yale University. The present volume is made up of a somewhat varied collection of papers dealing with different phases of mental growth and child training. The most interesting chapter, to us, was that on the training given her children by John Wesley's mother. For instance, her children were taught to read at the age of five: "One day was allowed the child wherein to learn its letters; and each of them did in that time know all its letters, great and small, except Molly and Nancy who were a day and a half before they knew them perfectly."

RACE PSYCHOLOGY. *A Study of Racial Mental Differences.*
By Thomas R. Garth
Whittlesey House (McGraw-Hill Book Co., Inc.)
$2.50 5½ x 8; xiv + 260 *New York*

A review of what is actually known about the comparative psychology of man. The author thinks that the evidence at present available is inadequate to establish the existence of real racial differences; even in the case of the intelligence tests, where the evidence is reasonably satisfactory that the actual I.Q.'s of, *e.g.*, the negro are lower than that of the whites, it is suggested that an unknown but possibly large part of the difference may be due to cultural and social factors, rather than to racial differences.

THE SIGNIFICANCE OF DELAYED REACTIONS IN YOUNG CHILDREN. *Comparative Psychology Monographs, Vol. 7, No. 4, Serial No. 34.*
By Magda Skalet *Johns Hopkins Press*
$1.50 6¾ x 10; 82 (paper) *Baltimore*

A study of the responses after a longer or shorter interval to such situations as the placing of a cookie under one of three dishes or the showing of one of a set of geometric forms. Some children, it was found, could remember the plate under which the cookie had been put for as long as 34 days. To anyone acquainted with children, this is an entirely credible result.

CHILD PSYCHOLOGY.
By Margaret W. Curti
Longmans, Green and Co.
$3.20 5¼ x 7¾; ix + 527 *New York*

This seems to us a sound and useful book on child psychology. The author holds what we think a well-balanced position on the whole environment-heredity question, which makes her discussion of such problems as the causes of juvenile delinquency of considerable value.

LE SOMMEIL.
By J. Lhermitte *Armand Colin*
10.50 francs (paper)
12 francs (cloth) 4⅜ x 6¾; 211 *Paris*

In this little book Dr. Lhermitte describes the physiological and psychological aspects of sleep.

DE OMNIBUS REBUS ET QUIBUSDEM ALIIS

A CENTURY WITH NORFOLK NAVAL HOSPITAL. 1830–1930. *A Story of the Oldest Naval Hospital, the Medical Department of the Navy and the Progress of Medicine Through the Past One Hundred Years.*
By Richmond C. Holcomb *Printcraft Publishing Co.*
$6.50 6 x 9¼; 543 *Portsmouth, Va.*

In this delightful book a former Medical Officer in Command of the Norfolk Naval Hospital turns historian. As is indicated in the subtitle, the book is by no means confined to the history of that institution. The narratives of the yellow fever epidemic of 1855 and of the battle between the *Virginia* and the *Monitor* will be found interesting. In the sketch of the state of medicine in 1830 is quoted a case history of "Paruria Erratica, or Uroplania," in which urine was discharged by the right and left ears, the left eye, the right and left breasts, and the navel. This is in its way as remarkable a case as that of the birth of Gargantua through his mother's left ear, recorded by the celebrated French physician Rabelais.

FADS, FRAUDS AND PHYSICIANS. *Diagnosis and Treatment of the Doctors' Dilemma.*
By T. Swann Harding *The Dial Press Inc,*
$3.50 5½ x 8⅛; 409 *New York*

This book will enrage all right-minded medical men, and will be quoted (unfairly) extensively by Christian Scientists and chiropractors. Very little in the present state of medicine, surgery, and pharmacy pleases the author. His documentation, mainly from the files of the professional journals, is extensive and impressive. The book would have been more effective if the author could have refrained from screaming quite so often.

Actually, of course, all is by no means well in medicine; the doctors themselves are frequently and considerably wrought up about conditions; but when a layman ventures to criticize, even if he merely repeat the remarks of doctors, he may be sure that the faculty will be upon him at once.

The author's remedy is State Medicine. He holds that turning the doctors into job-holders would make everything lovely. His optimism we cannot share.

LO!
By Charles Fort *Claude Kendall*
$2.50 5¼ x 8; 411 *New York*

This volume would have pleased Augustus de Morgan. The author holds that the earth is stationary; that the stars are volcanoes in a hollow sphere of land surrounding the earth; that frogs and snails fall in rainstorms; that earthquakes are caused by the appearance of new stars; and a good many other things. He has apparently devoted unlimited time to searching newspaper files for mysterious happenings. Unfortunately he rarely gives an adequate account; his method is one of enumeration of cases, not of analysis. The book will perhaps furnish a half-hour's entertainment.

THE ADVENTURE OF SCIENCE.
By Benjamin Ginzburg *Simon and Schuster*
$5.00 6 x 9; xvi + 487 *New York*

A popular history of science which plays the spot light successfully upon Pythagoras, Aristotle, Archimedes and Ptolemy, Copernicus, Galileo, Harvey, Newton, Lavoisier, Dalton, Faraday and Maxwell, Helmholtz, Lamarck and Darwin, Pasteur, Mendel and Einstein. The

book is well written and makes pleasant and easy reading.

THE GREEK ELEMENT IN ENGLISH WORDS.
By John C. Smock.
Edited by Percy W. Long
The Macmillan Co.
$15.00 $8\frac{3}{8}$ x $11\frac{1}{2}$; xiv + 356 *New York*

The desire of the author was to present "a volume of ponderable evidence that the Greek element in the English vocabulary has been underestimated." The evidence weighs 2200 grams. The list includes, we fear, what might be called padding, through the inclusion of Latin and other words with Greek suffixes, as *-ism,-ist,-ite*, etc.

SCIENCE AND THE SCIENTIFIC MIND
By Leo E. Saidla and Warren E. Gibbs
McGraw-Hill Book Co., Inc.
$3.00 $5\frac{1}{2}$ x 8; xiv + 506 *New York*

A collection of non-technical essays about science and its methods and purposes, designed as a text-book in English composition for students in technical schools. The material seems well chosen; and certainly one can but hope that the students who use the book will acquire some of the literary merits of the models offered them here.

THE ART OF GOOD LIVING. *A Contribution to the Better Understanding of Food and Drink together with a Gastronomic Vocabulary and a Wine Dictionary.*
By André L. Simon *Alfred A. Knopf, Inc.*
$2.50 $5\frac{1}{4}$ x 8; xii + 201 *New York*

This is a useful addition to gastronomic literature. It contains much sound advice on food and drink, and on what combinations are meritorious. Possibly not a book to recommend to American readers, except such as contemplate a trip to regions where the precepts of M. Simon can be more legitimately practiced.

DOCTORS AND SPECIALISTS. *A Medical Revue with a Prologue and a Good Many Scenes.*
By Morris Fishbein *Bobbs-Merrill Co.*
$1.00 5 x $7\frac{1}{2}$; xi + 118 *Indianapolis*

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